

## An Unusual Case of Virilizing Ovarian Tumor Associated With Carcinoma Insitu of Cervix

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**A**rrhenoblastoma or Sertoli-Leydig cell tumor is a rare androgen secreting ovarian tumor of unknown pathogenesis, has been reported to co-exist with other neoplasms of the female genital tract. Mostly benign, the tumor originates from the ovarian stromal sex cords, its tissue structure being similar to the Sertoli and Leydig testicular cells. Followed in detail, around one-fifth of these ovarian tumors are found to be malignant. We describe a case of slow growing Sertoli-Leydig cell tumor presenting with androgenic alopecia and virilization, associated with cervical carcinoma in-situ.

**Key Words:** Sertoli-Leydig cell tumor, Androgenic alopecia, Virilization, Carcinoma of cervix

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### Introduction

The Sertoli-Leydig cell tumor or arrhenoblastoma is a rare androgen secreting ovarian tumor of unknown pathogenesis, occurring more frequently in women of the reproductive age group. Indeed in a large series

75% cases occurred below the age of 30 years and only 10% occurred after 50 years of age<sup>1</sup>. Approximately one third to half of these show evidence of hyperandrogenism<sup>1,2</sup>. It is usually a benign tumor which originates from the ovarian stromal sex cords<sup>3</sup>, with a mixed tissue structure resembling the Sertoli and Leydig testicular cells. However on detailed clinical follow-up, up to 18% of these tumors were found to be malignant. Curiously co-existence with a variety of other female genital tract neoplasms has been described<sup>4-7</sup>. We report here an interesting patient with a Sertoli-Leydig cell tumor associated with cervical intraepithelial neoplasm, an association that has not been previously reported.

### Case report

A 43 year old woman presented with amenorrhea for 12 years, excessive facial hair growth and voice change for 5 years. She married at 18 years of age and had two children, with the last child birth at the age of 21 years. She had progressive oligomenorrhea leading on to amenorrhea with gradual masculinization of voice. There was also a gradual loss of scalp hair to a state of

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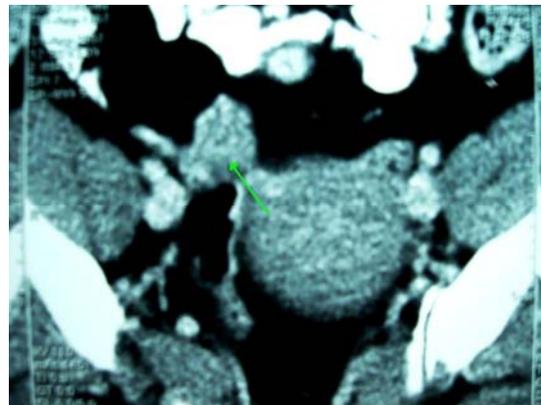
advanced baldness in the last 5 years. She has no history suggestive of thyroid dysfunction, diabetes mellitus or Cushing's syndrome. On examination the patient was obese (BMI-30.2 kg/m<sup>2</sup>), with female body contours, androgenic alopecia (Hamilton scale- VI) and hirsutism (Modified Ferriman and Gallwey score-30/36) (Fig. 1). There was no acanthosis, acne, clitoromegaly or breast atrophy. Clinical diagnosis of a hyperandrogenic disorder was arrived at. On investigating she was found to have impaired glucose tolerance. She was biochemically euthyroid with a normally suppressed overnight dexamethasone suppression test (serum cortisol: 1.3 µg/dL). Her serum testosterone was 12 ng/mL (normal <1.5 ng/mL), LH: 3.6 IU/L (normal: 0.5-5 IU/L), FSH: 0.4 IU/L (normal: 0.5-5 IU/L), estradiol: 136 pg/mL (normal: 30-250 pg/mL), prolactin: 7.6ng/mL (normal: 5-25pg/mL). Ultrasound abdomen and pelvis (trans-vaginal) showed normal adrenals, enlargement of right ovary (size 3.3×2.1 cm) and normal sized left ovary (0.9×1.7cm). Computerized tomography of abdomen and pelvis showed enlarged right ovary (3.3×2.2 cm) without any cystic lesions (Fig 2). Patient underwent total abdominal hysterectomy with bilateral salpingoophorectomy along with omental and iliac node sampling.



**Picture 1: Photograph showing hirsutism and baldness**

Grossly the right ovary (size 4×5 cm) exhibited multiple nodular lesions all of

which were well confined to the ovary. Microscopic examination showed the presence of nests of clear cells, some of them focally attempting to form tubular structures. The cells possessed nuclei, varying from small and round to large and pleomorphic vesicular type with anisonucleosis, open chromatin and prominent centromeres. There was significant presence of mitotic figures, over 20 per 10 high power field along with atypical mitotic figures and scattered tumor giant cells. These cells were merged with primitive gonadal stroma. Leydig cells were few in number. These findings were consistent with a poorly differentiated sex-cord stromal tumor of the Sertoli-Leydig cell type. Left ovary was essentially normal. The cervix showed cervical intra epithelial neoplasia (CIN-III) arising from surface squamous epithelium, as well as squamous metaplasia of the endocervical glands. The lymph nodes showed reactive changes without any evidence of metastasis. The post operative course was uneventful. Growth of facial and body hair decreased after removal of the ovarian tumor. Two months after surgery, serum testosterone was 2.9 ng/mL.



**Fig. 2: CT pelvis showing tumor arising from the right ovary (see arrow)**

## Discussion

Sertoli-Leydig cell tumor is a rare cause of androgenic alopecia, hirsutism and voice change.

There are very few reports of androgenic alopecia associated with Sertoli-Leydig cell tumor in literature<sup>8</sup>. In the present case, the symptom duration was for a period of 12 years. The virilizing effects of the tumor in the form of androgenic alopecia, voice change, and hirsutism were caused by elevation of testosterone synthesized by the tumor. The hormonal profile is dominated by the presence of high testosterone values and suppressed gonadotropins. The ultrasound examination of the ovaries is the diagnostic investigation of choice. When the tumor is too small to be detected by ultrasonography, unilateral high ovarian vein testosterone values (obtained by selective ovarian vein catheterization) confirms the diagnosis<sup>9</sup>. The differential diagnosis of Sertoli-Leydig cell tumor includes other causes of virilization such as exogenous androgen administration, Cushing's syndrome, virilizing adrenal tumor, congenital adrenal hyperplasia and hyperthecosis ovarii<sup>10</sup>.

The clinical and pathological features of 207 ovarian Sertoli-Leydig cell tumors were described by Young and Scully<sup>1</sup>. In this series the patients ranged in age from 2 to 75 (average 25) years. Seventy-five percent of them were 30 years of age or younger and less than 10% were over 50 years of age. One-third of the patients presented because of unequivocal evidence of androgen excess, and an additional 10% had a history suggesting androgen excess; most of the remaining patients complained of abdominal swelling or pain. Both ovaries were involved in 1.5% of the cases. The tumors ranged from microscopic to 51 cm in diameter (average 13.5 cm); 15% of them were ruptured. Thirty-eight percent of the tumors were solid, 58% were solid and cystic, and 4% were cystic. The solid tissue was typically lobulated and yellow. Follow-up was obtained for 164 patients. Tumors were clinically malignant in 18% of them.

Sertoli-Leydig cell tumor is more common during the reproductive years. In one extended

series<sup>11</sup> of 22 patients with Sertoli-Leydig cell tumors (n=15), Sertoli Cell tumors (n=2) and Leydig cell tumors (n=5); 16 of the 22 patients were in the reproductive age group, 5 were post-menopausal and only one occurred in a 4 year old child. The mean age of presentation in a series<sup>2</sup> of 23 patients was 34.5 years and ranged from 18-61 years. There was definite evidence of androgen production in 40% of the cases and suggestive evidence in an additional 10%. Irrespective of the age of onset, the clinical findings of severe, rapid virilization are frequently associated with a tumor source of androgens, Sertoli-Leydig cell tumor being the most frequent cause of a virilizing ovarian tumor. In over 90% of cases the tumor is unilateral<sup>11</sup>. Our case presented with a slow growing right ovarian tumor. On ultrasonographic evaluation of 15 patients with Sertoli-Leydig cell tumors these were either small (3-4 cm) or medium-sized (6-7 cm) solid tumors, or multilocular solid tumors of any size (3-18 cm) with purely solid areas mixed with areas of innumerable closely packed small cyst locules<sup>11</sup>.

Sertoli-Leydig cell tumors are solid tumors, with dimensions that correlate with the degree of differentiation; well differentiated tumors are under 0.5 cm, while poorly differentiated tumors can reach up to 10-15 cm; Sertoli-Leydig cell tumors under 5 cm are usually benign<sup>12</sup>. Rarely, Sertoli-Leydig cell tumor can be associated with other conditions like mucinous cystadenoma<sup>4</sup>, cervical sarcoma<sup>5</sup>, ovarian serous cystadenoma<sup>6</sup> or polycystic ovaries<sup>7</sup>.

The Sertoli-Leydig cell tumor is a slow growing functional ovarian tumor. In addition to virilizing symptoms and amenorrhea it may present with androgenic alopecia. Coincidental cervical carcinoma insitu has been noted.

Our case is unique as it is associated with cervical carcinoma in situ which has not been previously described in literature.

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