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CASE REPORT

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# Recurrent ovarian steroid cell tumour not otherwise specified: A case report

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**Abstract**

Steroid cell tumors not otherwise specified are one of the rare virilizing ovarian tumors. Most of the tumors are benign. This case report illustrates the challenge in managing steroid cell tumor not otherwise specified, which starts from determining its malignant potential, surveillance, and adjuvant treatment option.

**KEYWORDS**

malignant, steroid cell proliferation, virilizing ovarian tumor

## 1 | INTRODUCTION

Ovarian steroid cell tumor is considered a rare subtype of hormone-secreting ovarian tumor, accounting for about 0.1% of all ovarian tumors. We report a case of 39-year-old woman presented with progressively enlarging abdominal mass, with background history of virilization and amenorrhea for 5 years. She underwent an exploratory laparotomy, left salpingo-oophorectomy, infracolic omentectomy, and an appendectomy, with the histopathological report showing steroid cell tumor of the ovary, not otherwise specified. She was then treated for a low malignant potential tumor. However, after 1 year, there was recurrence with nodal metastasis and solitary liver nodule, requiring debulking surgery followed by adjuvant chemotherapy. This case report illustrates the challenge in managing steroid cell tumor not otherwise specified, which starts from determining its malignant potential, surveillance, and adjuvant treatment options.

The World Health Organization classification of ovarian sex cord-stromal tumors was revised in 2014. These tumors have been regrouped into three clinicopathological entities: pure stromal tumors, pure sex cord tumors, and mixed-sex cord-stromal tumors. Steroid cell tumor is one of the tumor entities classified under pure stromal tumors. It is an uncommon neoplasm, accounting for only 0.16% of all ovarian tumors. These are defined as an ovarian neoplasm compound made up entirely of cells that resemble steroid-secreting cells but without Reinke crystals.[1]

Steroid cell tumor not otherwise specified (NOS) is the most common variety of steroid cell tumors, besides other

less common tumors, namely Leydig cell tumor and stromal luteoma. Androgenic manifestation was observed in 41% of patients, whereas hyperestrogenic and hypercortisolism features were reported in some cases.[2]

Most of the tumors were benign and unilateral.[2] The tumor's malignant behavior can be observed clinically and predicted through its pathological examination. Due to its rarity, no clear consensus of standard treatment has been described, and disease management remains individualized.

In this study, we reported a steroid cell tumor case not otherwise specified in a woman at a reproductive age who had a unilateral ovarian tumor during the first presentation. She was treated with fertility-preserving primary surgery. However, she suffered a recurrence of the disease, that is, to her lymph nodes and liver, after 12 months and required another surgery for tumor debulking followed by adjuvant chemotherapy.

## 2 | CASE REPORT

A 38-year-old married but nulliparous woman presented 3 months of abdominal distension and amenorrhea and virilization for the past 5 years. Examination revealed that she is obese, with hirsutism and male pattern alopecia besides a palpable pelvic mass of 14 weeks of gravid uterine size. Her test results showed that her testosterone level (52.1 nmol/L) was high, her estradiol level (159.8 pg/L) was low, and her level of follicle-stimulating hormone (<0.3 IU/L) was low; moreover, luteinizing hormone (<0.13 IU/L) was also observed. Ca125 was the only tumor marker that increased significantly (479.2 IU/L), while carcinoembryonic antigen (CEA) and Ca19.9 were normal. She did not have any other risk factors for ovarian tumors besides being obese and nulliparous.

Her computed tomography (CT) scan confirmed a pelvic mass likely from the ovary with no evidence of disease elsewhere. The patient then underwent an exploratory laparotomy, in which, intraoperatively, the tumor was confined to the left ovary with no evidence of disease spread to adjacent organs, the peritoneum, and lymph nodes. Left salpingo-oophorectomy, infracolic omentectomy, and appendectomy were also performed; further, her histopathological examination reported a steroid cell tumor of the left ovary, NOS. The tumor's gross appearance was brownish with an irregular surface, in which an open cut revealed a patchy yellowish hemorrhage area. Microscopic examination revealed that the tumor comprised uniform plump cells with round nuclei and abundant granular eosinophilic cytoplasm with no cellular atypia. Focally, the tumor cell shows clear cytoplasm. They are arranged in lobules and packed trabecular formations with intervening vascular septa of varying thickness. Mitosis is inconspicuous. No apparent Reinke crystal was seen. There were areas of granulation tissue formation and necrosis. Calcification and hemorrhage were also noted. Moreover, the tumor did not involve the left fallopian tube, omentum, and appendix. Prognostically, she was treated for a low malignant potential tumor, which follows a benign clinical course, with regular 4 monthly surveillance at our clinic.

However, recurrence was noted after 1 year when palpable abdominal mass was found during one of her routine check-ups, as evidenced by her high testosterone levels. Her CT scan also showed mesenteric and pelvic nodal metastasis measuring 6.7 cm × 6.7 cm × 5.7 cm, indenting onto the sigmoid colon, and a solitary liver nodule measuring 3.5 × 3.7 cm at segment V. After a multidisciplinary team discussion involving the hepatobiliary, colorectal, and gynecology teams, she was subjected to another surgery, where exploratory laparotomy, adhesiolysis, and debulking of the tumor with right hemihepatectomy, cholecystectomy, and sigmoid colectomy were performed. Histopathology examination of the sample during the surgery confirmed a metastatic steroid cell tumor. The surgery was complicated by surgical wound breakdown, which required secondary suturing. However, she recovered well after 3 weeks postsurgery.

She was then subjected to adjuvant chemotherapy with a combination of bleomycin, etoposide, and platinum regimen for four cycles. She responded well with the chemotherapy, whereby no evidence of disease recurrence was noted post-completion of the treatment. She remains at a good functional status and disease-free for 3 months till now.

## 3 | DISCUSSION/CONCLUSION

Women with a pelvic mass and virilizing signs strike a diagnosis of an androgen-secreting tumor of the ovary. It is identified as a group of tumors arising from the sex cord and stromal cell, causing the overproduction of steroid hormones such as androgen, estrogen, or precursors. Steroid cell tumor of the ovary is one of the subtypes of hormone-secreting ovarian tumor. It is rare, accounting for about 0.1% of all ovarian tumors.[1]

In a study conducted by Hayes et al[2], the mean age of presentation for steroid cell tumor is 43 years, in which if presented in patients aged 51 years or older, the possibility of the tumor to be malignant is higher. Otherwise, there are no other specific risk factors associated with steroid cell tumor illustrated in literatures.

Hyperandrogenism secondary to ovarian tumors can mostly result in a significantly elevated testosterone level with sometimes normal dehydroepiandrosterone.[3] Hyperandrogenism occurs in more than 50% of steroid cell tumors not otherwise specified (NOS).[2,4] Clinical presentations may vary according to the age of the patient. Children with this tumor may have heterosexual precocious puberty. In contrast, adults can have hoarseness of voice,

acne, hirsutism, male pattern alopecia, clitoromegaly, loss of female fat distribution, irregular menses, and amenorrhea. [3,5] Virilizing signs in steroid cell tumors, NOS, are usually slowly progressive, unlike other androgen-secreting tumors wherein their signs are more rapidly developed. [3,6] Hyperestrogenism was also reported in 6% to 23% of cases, giving rise to symptoms such as menorrhagia, postmenopausal bleeding, and even endometrial carcinoma. [2] Moreover, about 6%-10% of these patients were determined to present Cushing's syndrome due to excess cortisol production.[2,7]

The majority of the steroid cell tumor appears solid or mostly solid on imaging. Calcification is not commonly seen within the tumor and is usually not associated with ascites.[8] Ultrasound and CT scans have been the imaging modalities widely used in ovarian tumors. However, magnetic resonance imaging has been shown to have the diagnostic value for tumors with lipid components.[9]

The tumor's gross appearance is well-circumscribed and solid, with a yellowish cut surface appearance due to its fat component. [2,6] Hayes and Scully et al reported 63 cases of steroid cell tumors, elaborating five important macroscopic and microscopic features suggesting malignancy. Malignant behavior is often observed in tumors of greater than 7 cm diameter in 78% of cases and presence of necrosis and hemorrhage in 86% and 77% of cases, respectively. Microscopic features of a malignant tumor are the most reliable; their pathologic presence correlates with two or more mitotic figures per 10 high-power fields, which is observed in 92% of malignant tumors, whereas nuclear atypia of grades 2 and 3 is seen in 64% of malignant tumors. [2]

It is essential to distinguish steroid cell tumors NOS from other steroid cell tumor types. Leydig cell tumor typically has Reinke crystals in the cytoplasm. Luteoma is often recognized by its location within the ovarian stroma and with stromal hyperthecosis.[10] Meanwhile, pregnancy luteoma is a non-neoplastic lutein proliferation secondary to human chorionic gonadotrophin stimulation, with prominent mitotic activity without nuclear atypia, which involutes after pregnancy. [2] Luteinized thecoma can be identified by the presence of predominant spindle cell background, while in the steroid cell, NOS luteinization is rare. On the other hand, clear cell carcinoma is composed exclusively of a clear cell with glycogen-rich cytoplasm and typically eccentric nuclei compared with the lipid-filled cytoplasm and central nuclei in the steroid cell tumor.[2]

Most of the cases are confined to unilateral ovaries and diagnosed at an early stage. In 20% of cases, local metastasis was reported, with the peritoneal cavity being the most common area. [2] While distant metastasis is rare, there were cases reported to have extensive bone metastasis. [11] Staging laparotomy has remained as the mainstay of management, where total hysterectomy and bilateral salpingo-oophorectomy are recommended in most cases, with tumor debulking in advanced diseases. For young women with early-stage disease, unilateral salpingo-oophorectomy has been determined adequate as bilateral ovarian involvement occurs only in 6% of cases. [2] Surveillance of the disease postsurgery is essential and should include the measurement of the hormone level, particularly those that increase before surgery. [2]

The value of adjuvant chemotherapy and radiotherapy treatment was poorly understood due to the rarity of the tumor metastasis and recurrence. The various chemotherapy regimens reportedly used were bleomycin, etoposide, and cisplatin; docetaxel and nedaplatin; cyclophosphamide; single-agent cisplatin; doxorubicin, cyclophosphamide, and cisplatin; vincristine, actinomycin D, and cisplatin; and cyclophosphamide, cisplatin, doxorubicin, and 5-fluorouracil. The best regimen has not yet been established, with most cases reporting poor outcomes.[2,10] Radiation therapy was mentioned in few cases where it was given postoperatively for abdominal recurrence. In another case, it was given preoperatively to the liver metastasis to achieve optimal cytoreduction.[2] In both cases, radiation therapy was reported to have a promising role and should be explored further.

In the mid-1990s, Pasca et al[11] demonstrated that androgen-secreting tumors were dependent upon continuous gonadotrophin stimulation. This report supports the usage of gonadotrophin-releasing hormone agonist (GnRHa) to suppress ovarian steroidogenesis. Serum testosterone level has been shown to revert to normal level after treatment with GnRHa in patients with residual tumor postsurgery. They also reported the virilization features significantly.[12,13] It has also been used as adjuvant therapy following primary surgery, with a monthly injection for 6 months, as reported by Dong-Hae et al.[14] It has been reported to reduce the size of the tumor by 34.3% in recurrent disease. [12] Meanwhile, mitotane is another drug that has been determined to suppress ovarian steroidogenesis. It has been proven to reduce the cortisol level formerly used in adrenocortical malignancy and Cushing's syndrome. It has been described to be used in ovarian steroid cell tumor with hypercortisolism, bearing a good response. [15]

In conclusion, recurrent ovarian steroid cell tumor NOS is considered rare. This case shows how benign tumors can have malignant potential and present as a recurrent tumor. Thus, carefully assessing its malignant potential at first presentation using the criteria suggested by Hayes and Scully[2] in 1897 may help determine this tumor's clinical outcome. Surgical tumor debulking is still the mainstay of treatment, aiming for complete cytoreduction. Adjuvant chemotherapy or radiotherapy is advisable for tumors with metastasis and recurrence, while GnRHa can be considered in those not suitable for surgery and second-line treatment. Thus, monitoring of the disease is mandatory, by not just clinical surveillance but also serial hormonal level assessment.

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## CONFLICT OF INTEREST

None declared.

## AUTHOR CONTRIBUTIONS

AAbMJ: took part in the writing and editing this case report. AB.: took part in writing the initial draft of the case report. MM, MA, IA, and MRMN: managing and following the patient up in gynecology team, had full access to all of the data in the case report, and took responsibility for the integrity of the data participated in the data collection and writing of the article. MNY and VCJY: participated in the design and proofreading of this article.

## ETHICAL APPROVAL

This article is published with consent of the patient and approved for publication by the Medical Research and Ethics Committee, Ministry of Health, Malaysia.

## DATA AVAILABILITY STATEMENT

The data are available on the basis of Gynae-oncology Unit, Department of Obstetrics and Gynaecology Hospital Sultanah Bahiyah, Alor Star, Kedah, Malaysia.

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