

Contrast-enhanced ultrasound of ovarian steroid cell tumor, not otherwise specified: A case report

MAI SUN¹ and BO ZHANG¹⁻³

¹Department of Ultrasound, China-Japan Friendship Hospital; ²National Center for Respiratory Medicine, National Clinical Research Center for Respiratory Diseases, Institute of Respiratory Medicine of Chinese Academy of Medical Sciences, Beijing 100029; ³Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, P.R. China

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Abstract. Ovarian steroid cell tumor is a rare type of ovarian tumor, accounting for ~0.1% of all neoplasms of the ovary. Patients suffering from this type of tumor exhibit virilization due to high testosterone levels. The present study reported a case of an elderly female patient with high testosterone serum levels, resulting in hirsutism and deepening of the voice. Magnetic resonance imaging did not reveal any solid ovarian tumor. However, gray-scale ultrasound indicated suspicious solid nodules on the right ovary. A clear outline of the tumor, characterized by ring-shaped uniform enhancement, was revealed by contrast-enhanced ultrasound (CEUS) scanning. In addition, laparoscopic resection of both fallopian tubes and ovaries confirmed the right ovarian steroid cell tumor. After the operation, the patient's symptoms were completely relieved and testosterone levels returned to normal. In the present study, a case of ovarian steroid tumor diagnosed by CEUS was reported, supporting the significant role of CEUS in the detection of adnexal tumors.

Introduction

Ovarian steroid cell tumor is a rare subtype of sex-cord tumor, accounting for ~0.1% of all ovarian neoplasms (1). Among all types of ovarian steroid cell tumor, steroid cell tumor, not otherwise specified (NOS), is the predominant type, accounting for ~80% of all cases (2). This type of tumor may occur at any age, with a mean age of 43 years. Steroid cell tumors most commonly secrete androgens, thus resulting in virilization and hirsutism (1). Although the majority of these tumors are benign, approximately one-third of them may display a malignant

behavior (2). Ultrasound and magnetic resonance imaging (MRI) are the most commonly applied imaging methods for steroid cell tumors. However, histopathology remains the gold standard technique for tumor diagnosis. A recently used imaging method, namely contrast-enhanced ultrasound (CEUS), uses microbubble contrast agents for imaging. It has been reported that CEUS may be used to improve the diagnostic accuracy of ovarian tumor ultrasonography (3). In the current study, a case of a female patient with ovarian steroid cell tumor diagnosed using CEUS was reported.

Case report

A 61-year-old female was admitted to the China-Japan Friendship Hospital (Beijing, China) with complaints of a male patterned voice and hirsutism for >3 years. The patient also reported unexpected hyperhidrosis that persisted since it developed two years previously. The patient's BMI was normal but after walking for 10 min, the patient was sweating profusely. Physical examination revealed normal blood pressure, obvious facial hair and low voice. In addition, laboratory tests indicated high testosterone (21.690 nmol/l; normal range, 0.35-2.60 nmol/l) and normal dehydroepiandrosterone (39.70 µg/dl; normal range, 12-133 µg/dl) levels in the serum. The other laboratory tests, including cortisol and thyroid-stimulating hormone levels, and tumor markers, such as serum CA125, carcinoembryonic antigen, CA199, CA153 and alpha-fetoprotein levels, were in the normal range. Finally, pelvic MRI revealed that the right ovary was normal.

The patient underwent conventional ultrasound for routine examination. A high-resolution ultrasound instrument (Siemens Acuson Sequoia; Siemens Medical Solutions) equipped with a 10 MHz linear probe was used. A suspicious homogeneous iso-echoic lesion with a size of 1.7x1.5 cm was detected in the right ovary on the gray-scale ultrasound (Fig. 1A). However, color Doppler ultrasound indicated no blood flow signal in the lesion (Fig. 1B).

To verify the diagnosis, the same ultrasound system (Siemens Acuson Sequoia; Siemens Medical Solutions) equipped with a 10 MHz linear probe was used for CEUS examination. Low mechanical index CEUS was performed

Correspondence to: Dr Bo Zhang, Department of Ultrasound, China-Japan Friendship Hospital, 2 Yinghua East Road, Beijing 100029, P.R. China
E-mail: zora19702006@163.com

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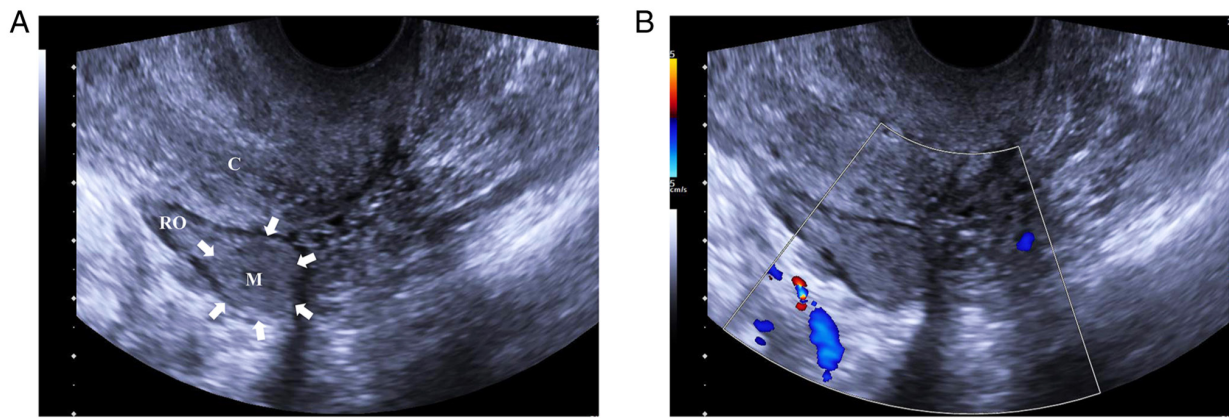


Figure 1. Transvaginal ultrasonography of right ovary. (A) Gray-scale ultrasound indicating a suspicious homogeneous iso-echoic lesion (arrows) with a size of 1.7x1.5 cm in the right ovary. (B) Color Doppler flow imaging indicated no blood flow signal in the lesion. RO, right ovary; C, cervix; M, mass.

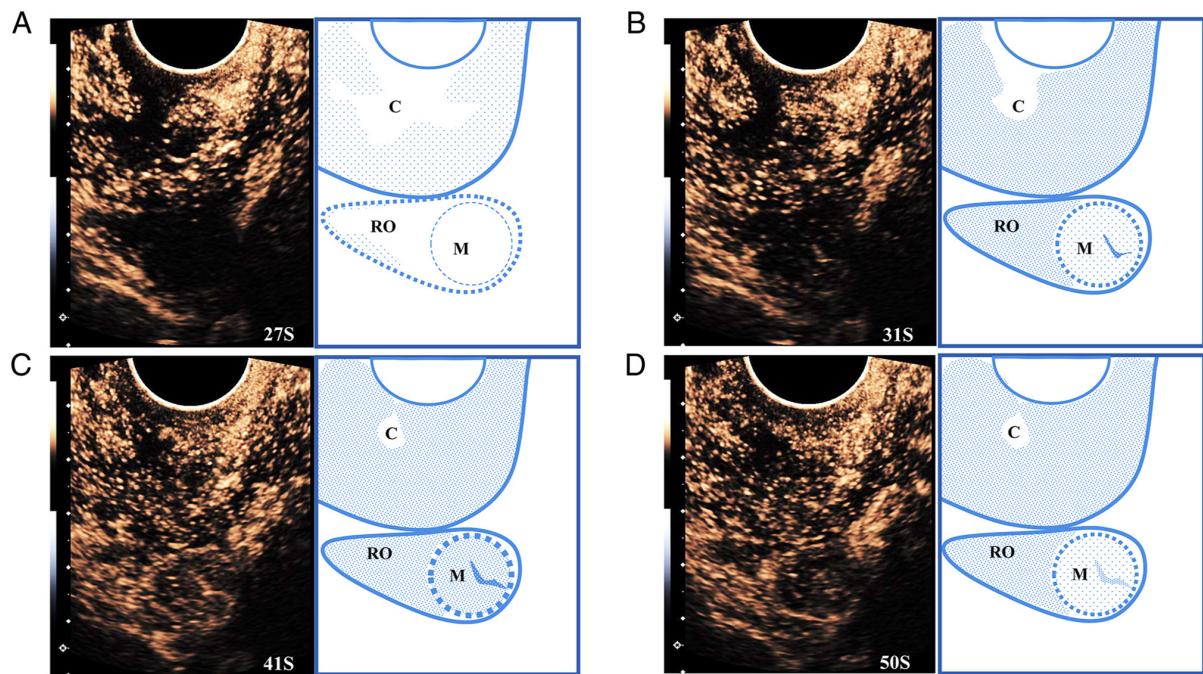


Figure 2. CEUS findings of the ovarian steroid cell tumor in the right ovary. (A) Microbubbles were first detected at 27 sec. (B) The branch blood vessel structure is visible in the center. (C) CEUS image obtained at 41 sec after contrast injection indicating an iso-enhancement nodule with ring-shaped enhancement in the arterial phase. (D) CEUS image obtained at 50 sec after contrast injection indicate persistent iso-enhancement of the nodule (arrow) in the late phase. The drawings to the right of the CEUS images are schematics of the CEUS findings. C, cervix; RO, right ovary; M, mass; CEUS, contrast-enhanced ultrasound.

after a bolus intravenous injection of 1.2 ml SonoVue® (Bracco) followed by a flush of 5 ml saline. Following injection, a timer was started. During the arterial phase, the masses appeared iso-homogeneous compared with the peripheral ovarian parenchyma and maintained their iso-enhancement in the late phase. The lesion was enhanced at the beginning of the arterial phase from the center to the periphery, characterized by ring-shaped enhancement (Fig. 2).

Due to the findings of CEUS, a testosterone-producing ovarian tumor was suspected. Therefore, the patient underwent laparoscopic bilateral salpingo-oophorectomy. Histopathological assessment confirmed the presence of a steroid cell tumor in the right ovary with a diameter of 1.5 cm.

The analysis also revealed mild atypia and no significant necrosis or mitotic activity. In addition, immunohistochemical staining indicated strong and diffuse staining for inhibin and calretinin (Fig. 3). The analyses were performed at the pathology department according to standard procedures using the following reagents according to the manufacturer's protocol: Inhibin alpha mouse monoclonal antibody (cat. no. ZM-0460; Origene); and calretinin mouse monoclonal antibody (cat. no. MAB-0716; MAB Biotechnologies).

Postsurgical evaluation after one month revealed normalization of testosterone levels to 0.910 nmol/l, while the patient experienced complete symptomatic relief. At 12 months postoperatively, the female patient had no evidence of recurrence.

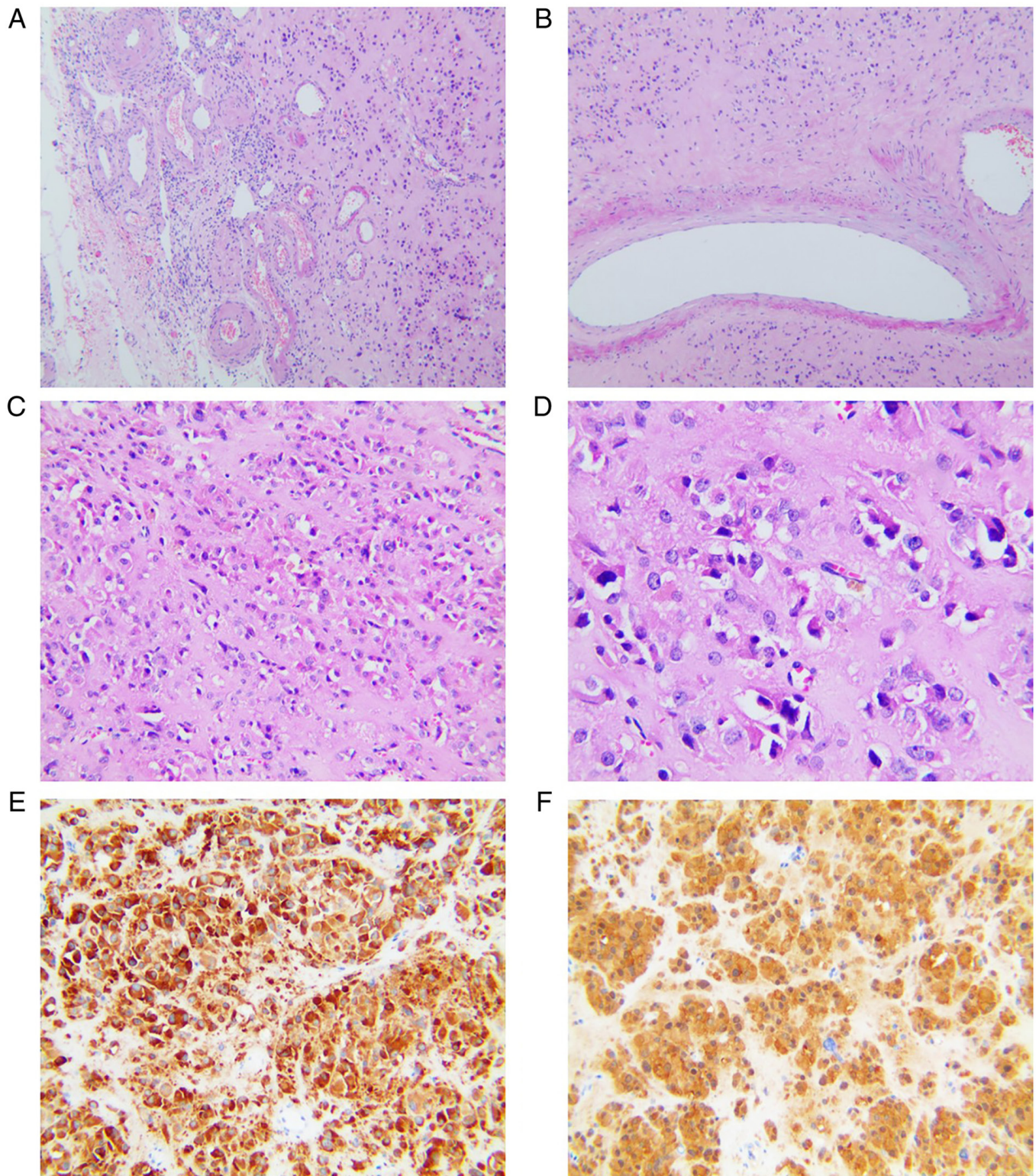


Figure 3. Histological and immunohistochemical characterization of the ovarian steroid cell tumor in a 64-year-old female patient. (A and B) Histopathology indicated (A) abundant vascular structure at the tumor margin and (B) thick blood vessels inside the tumor (H&E; magnification, x100). (C and D) Histopathology indicated mild atypia. There was an absence of necrosis and mitosis. (C) H&E (magnification, x200); (D) H&E (magnification, x400). (E and F) Immunohistochemistry indicated positivity for (E) inhibin α and (F) calretinin (magnification, x200).

Discussion

The incidence of steroid cell tumors is estimated to be <0.1% among all types of ovarian tumor (1). Steroid cell

tumor is an ovarian parenchymal tumor composed of steroid cells (2). This type of tumor may occur at any age, with an average age of 43 years (1). The clinical manifestations of the disease are associated with the type of hormones

secreted by the tumors. The majority of them secrete testosterone. Patients with steroid cell tumors have virilization symptoms such as hirsutism, acne, amenorrhea, deep voice, abnormal facial hair growth and at times alopecia (1,4,5). In addition, in postmenopausal females, manifestations of estrogen-secreting tumors include endometrial hyperplasia and bleeding. Rarely, progestational effects or Cushing's syndrome may occur (1,6). Steroid cell tumors have also been reported in patients with von Hippel-Lindau syndrome (7-9).

Steroid cell tumors are most commonly solid, benign, unilateral and well-circumscribed. However, mixed solid and cystic masses may also be seen (10). Histologically, steroid cell tumors consist of polygonal cells (2), while calcification, necrosis and hemorrhage may be occasionally observed. Nuclear atypia and mitotic activity are rare. As mentioned above, ovarian steroid cell tumors are benign. However, approximately a third of these tumors may exhibit malignant behavior. Hayes and Scully (1) defined five pathological predictive characteristics of the malignant behavior of these tumors: size >7 cm; >2 mitoses/10 high-power fields; necrosis; hemorrhage; and grade 2-3 nuclear atypia (11,12). Immunohistochemically, inhibin and calretinin are considered sensitive markers for diagnosing steroid cell tumors.

In the clinic, surgery is the basic treatment approach for ovarian steroid tumors. Treatment is individualized and depends on several factors, including tumor stage, the presence of malignant features, age and fertility status (13,14). Following surgery, testosterone levels may return to normal, while virilization symptoms disappear. The prognosis of ovarian steroid tumor is good, while metastasis and recurrence rarely occur.

The most commonly used imaging techniques for this type of tumor are ultrasound and MRI. As demonstrated by transvaginal ultrasound, ovarian steroid cell tumors are solid tumors with a hypo-/iso-echoic, homogeneous or heterogeneous texture (10,15-17), characterized by abundant blood flow signals (18). On MRI, steroid cell tumors appear heterogeneous and as medium-intensity solid mass interspersed with small cysts. The tumor is significantly enhanced following Gd-diethylene triamine pentaacetate injection, thus indicating hypervascularity of the tumor (6,16,19).

Certain tumors may be so small that they may not be diagnosed even after careful radiological scrutiny (17,20). In the case of the present study, no obvious mass was observed on the right ovary on MRI. However, a suspicious mass was observed on gray-scale ultrasound. The tumor was not definitively diagnosed by conventional ultrasonography due to its small size and isoechoic appearance on gray-scale ultrasonography compared with the ovarian tissue. Finally, CEUS revealed a solid mass in the ovary with clear boundaries. Furthermore, color Doppler imaging indicated no blood flow signals in and around the tumor. However, using CEUS, internal dendritic and peripheral annular enhancements were observed, which may have been due to the feeding vessels within the tumor and the abundant vascular structures around it. The CEUS findings were consistent with the histopathological results. To the best of our knowledge, the present study was the first

case study to describe the contrast-enhanced appearance of a steroid cell tumor. It has been reported that the use of a contrast agent may improve the clarity of the power Doppler signal and help identify the vascularized areas of a tumor. CEUS is able to clarify the location of a tumor, whose lesions cannot be displayed by gray-scale ultrasound and MRI. CEUS is not a specialized imaging method for NOS. However, it is able to improve the specificity of ultrasound in the differential diagnosis through dynamic microvascular features. Therefore, the features of CEUS may improve the diagnostic accuracy. At present, the definitive diagnosis of ovarian steroid tumors is made based on histopathological evaluation and immuno-histochemistry (21).

Steroid cell tumors are characterized by a slightly abundant blood supply. The present case study reported the CEUS appearance of an ovarian steroid tumor and highlighted the significance of CEUS in the detection of these types of tumors. Furthermore, the imaging features of CEUS may provide useful information regarding the tumor location, density and enhancement pattern.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

MS and BZ performed examinations and recorded data. MS collected clinical information and drafted the manuscript. MS and BZ approved the final version of the manuscript for publication. MS and BZ checked and approved the authenticity of the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the China-Japan Friendship Hospital (Beijing, China). Written informed consent was provided by the patient.

Patient consent for publication

The patient provided written informed consent for the publication of her data and images.

Competing interests

The authors declare that they have no competing interests.

References

- Hayes MC and Scully RE: Ovarian steroid cell tumors (not otherwise specified). A clinicopathological analysis of 63 cases. *Am J Surg Pathol* 11: 835-845, 1987.
- Herrington CS (ed): WHO Classification of Tumours Female Genital Tumours. International Agency for Research on Cancer, 2020.
- Ma X, Zhao Y, Zhang B, Ling W, Zhuo H, Jia H and Li P: Contrast-enhanced ultrasound for differential diagnosis of malignant and benign ovarian tumors: Systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 46: 277-283, 2015.
- Liu AX, Sun J, Shao WQ, Jin HM and Song WQ: Steroid cell tumors, not otherwise specified (NOS), in an accessory ovary: A case report and literature review. *Gynecol Oncol* 97: 260-262, 2005.
- Dinc G, Saygin I, Kart C, Mungan S, Guven S and Seda Güvendağ Güven E: A rare case of postmenopausal severe virilization: Ovarian steroid cell tumour, not otherwise specified. *J Cases Obstet Gynecol* 3: 19-21, 2016.
- Wang PH, Chao HT, Lee RC, Lai CR, Lee WL, Kwok CF, Yuan CC and Ng HT: Steroid cell tumors of the ovary: Clinical, ultrasonic, and MRI diagnosis-a case report. *Eur J Radiol* 26: 269-273, 1998.
- Morani AC, Mubarak AI, Bhosale HR, Ramani NS, Waguespack SG and Ying A: Steroid cell ovarian tumor in a case of von Hippel-Lindau disease: Demonstrating lipid content of the mass with MR imaging. *Magn Reson Med* 18: 251-252, 2019.
- Wagner M, Browne HN, Linehan WM, Merino M, Babar N and Stratton P: Lipid cell tumors in two women with von Hippel-Lindau syndrome. *Obstet Gynecol* 116: 535-539, 2010.
- Marques A and Portugal R: Ovarian steroid cell tumor in an adolescent with Von Hippel-Lindau syndrome: A case report and review of the literature. *Int J Gynecol Pathol* 39: 473-477, 2020.
- Patil VS, VemiReddy PR, Taqdees A and Arakeri SU: Steroid cell tumor of the ovary-a rare case report and review of literature. *Int J Appl Basic Med Res* 9: 185-187, 2019.
- del Valle Rubido C: Ovarian steroid cell tumor associated to endometrial hyperplasia and presenting as post-menopausal vaginal bleeding. *Gynecol Obstet (Sunnyvale)* 5: 316, 2015.
- Yoshimatsu T, Nagai K, Miyawaki R, Moritani K, Ohkubo K, Kuwabara J, Tatsuta K, Kurata M, Fukushima M, Kitazawa R, *et al*: Malignant ovarian steroid cell tumor, not otherwise specified, causes virilization in a 4-year-old girl: A case report and literature review. *Case Rep Oncol* 13: 358-364, 2020.
- Jiang W, Tao X, Fang F, Zhang S and Xu C: Benign and malignant ovarian steroid cell tumors, not otherwise specified: Case studies, comparison, and review of the literature. *J Ovarian Res* 6: 53, 2013.
- Ismail S, Hraib M, Issa R, Alassi T and Alshehbi Z: A large ovarian steroid cell tumor-not otherwise specified with a unique combination of benign and malignant features as a challenging cause of oligomenorrhea and hirsutism in a 21-year-old Syrian female: A case report. *BMC Womens Health* 21: 95, 2021.
- Matsuda S, Yamaguchi Y, Kaseki H, Watanabe K, Ono S, Yamamoto A, Ichikawa M, Akira S and Takeshita T: Case of ovarian steroid cell tumor diagnosed after presenting acute heart failure. *J Obstet Gynaecol Res* 46: 1211-1215, 2020.
- Matsukawa J, Takahashi T, Hada Y, Kameda W, Ota K, Fukase M, Takahashi K, Matsuo K, Mizunuma H and Nagase S: Successful laparoscopic resection of virilizing ovarian steroid cell tumor, not otherwise specified, in a 22-year-old woman: A case report and evaluation of the steroidogenic pathway. *Fukushima J Med Sci* 65: 133-139, 2020.
- Faten H, Dorra G, Slim C, Wajdi S, Nadia C, Kais C, Tahia B and Mohamed A: Ovarian steroid cell tumor (Not Otherwise Specified): A case report of ovarian hyperandrogenism. *Case Rep Oncol Med* 2020: 6970823, 2020.
- Jiang MJ, Le Q, Yang BW, Yuan F and Chen H: Ovarian sex cord stromal tumours: Analysis of the clinical and sonographic characteristics of different histopathologic subtypes. *J Ovarian Res* 14: 53, 2021.
- Saida T, Tanaka YO and Minami M: Steroid cell tumor of the ovary, not otherwise specified: CT and MR findings. *AJR Am J Roentgenol* 188: W393-W394, 2007.
- Schecker EV, Kathuria A, Esnakula A, Sasano H, Yamazaki Y, Tevosian S, Auchus RJ, Ghayee HK and Dhir G: Expression of key androgen-activating enzymes in ovarian steroid cell tumor, not otherwise specified. *J Investig Med High Impact Case Rep*: Jun 26, 2020 (Epub ahead of print).
- Sconfienza L, Perrone N, Delnevo A, Lacelli F, Murolo C, Gandolfo N and Serafini G: Diagnostic value of contrast-enhanced ultrasonography in the characterization of ovarian tumors. *J Ultrasound* 13: 9-15, 2010.



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