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Adult-Type Granulosa Cell Tumor with Similar Clinical Findings Seen during Ovarian Cystectomy Performed at the Same Time as Laparoscopic Ovarian Drilling for Polycystic Ovarian Syndrome: An Extremely Rare Case

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Abstract

Polycystic ovary syndrome (PCOS) is a major cause of anovulatory infertility. Laparoscopic ovarian drilling (LOD) is a treatment for PCOS that allows the laparoscopic identification of other intra-abdominal lesions and the provision of diagnostic treatment. This study reports a case of PCOS with an ovarian mass in which LOD was aggressively used and a granulosa cell tumor (GCT) was found. A 34-year-old woman with secondary amenorrhea and irregular menstrual cycles presented to the emergency department with abdominal pain of unknown etiology. Imaging studies revealed a 6-cm left ovarian mass with an internal appearance suggestive of a hemorrhage. The patient's secondary amenorrhea was subsequently diagnosed as PCOS, and LOD was performed to preserve her fertility. Simultaneously, a cystectomy was performed to evaluate the tumor in the left ovary; the diagnosis was adult-type GCT. Although concomitant GCT and PCOS are extremely rare, the two conditions have similar clinical manifestations. In women of reproductive age, the impact of surgery on future fertility should be considered, and the initial surgical technique should be chosen carefully.

Keywords

Polycystic Ovary Syndrome, Laparoscopic Ovarian Drilling, Granulosa Cell Tumor

1. Introduction

Polycystic ovary syndrome (PCOS), which occurs in 5% - 10% of women of reproductive age, is associated with abnormal menstruation and infertility due to ovulatory dysfunction [1] [2]. PCOS is characterized by high luteinizing hormone (LH), androgen, and anti-Müllerian hormone (AMH) levels, which suppress follicle development [2]. Regarding the association between PCOS and ovarian tumors, an increased risk of ovarian cancer and serous borderline tumors of the ovary has been reported in postmenopausal women [3]; therefore, we believe that drawing attention to the occurrence of ovarian cancer and tumors in PCOS is imperative [4] [5].

Granulosa cell tumors (GCT) are rare sex cord stromal tumors that account for approximately 2% of ovarian malignancies [6]. Most affected women are menopausal at the time of presentation [7]. However, GCT can also occur in younger patients, making fertility preservation important. GCT are often stage I, meaning that they are confined to a unilateral ovary [8]; in such cases, the contralateral ovary and uterus may be targeted for fertility-sparing surgery (FSS). The prognosis is almost always good, with a 5-year survival rate of 97% - 98% [7] [9] [10], but many cases of late recurrences occur 20 years or more after diagnosis [6]; therefore, long-term follow-up is necessary.

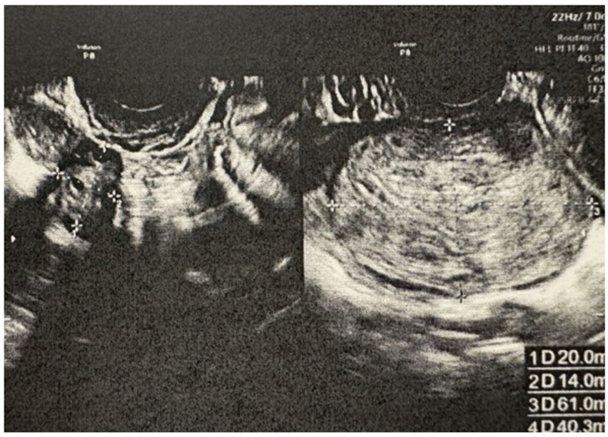
In the present study, we encountered an extremely rare case of adult-type granulosa cell tumor (AGCT) after cystectomy performed simultaneously with laparoscopic ovarian drilling (LOD) for PCOS. It is important to recognize that PCOS and GCT have similar clinical findings and occur simultaneously. In addition, preoperative counseling, including fertility preservation, is extremely important.

2. Case Report

Here we report the case of a 34-year-old woman who was judged to have typical PCOS as evidenced by high LH and AMH levels. As a result, suspected ovarian hemorrhage with lower abdominal pain was treated as a simple complication. Because we treated the ovarian tumor image primarily in response to PCOS, we did not consider the possibility of ovarian tumors with similar hormonal changes. As a result, we had to perform a burdensome surgery on the infertility patient.

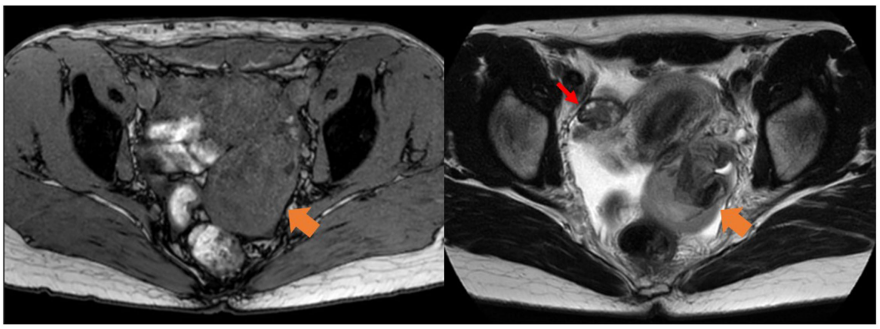
She had been taking low-dose oral contraceptives for 3 months for secondary amenorrhea and irregular menstrual cycles. Ten days after taking the pills, she experienced lower abdominal pain and visited her local physician, who suspected ovarian hemorrhage. Due to persistent pain, she visited her doctor's office again and was referred to our hospital's emergency department with suspected torsion of the ovarian tumor. At our hospital, transvaginal ultrasonography revealed a normal-sized uterus with a 2.1-mm endometrium and no thickening, a normal-sized right ovary (20 × 14 mm), and an enlarged left ovary (61 mm). Inside the ovary, a spongy mass with a rather solid appearance was observed sug-

gestive of a hemorrhage (Figure 1). The tumor marker cancer antigen 125 (CA125) and cancer antigen 19-9 (CA19-9) levels were normal. Pelvic magnetic resonance imaging (MRI) showed a well-defined 58-mm mass with low to equal signaling on T1-weighted imaging (T1WI) and mixed mild high and low signals on T2-weighted imaging (T2WI) in the left adnexal region, suggesting an intraovarian hematoma. No thickening of the capsule or nodules was noted, and aggressive malignancy was not suspected (Figure 2(a), Figure 2(b)).



(a) (b)

Figure 1. Ultrasound imaging of the (a) right ovary and (b) left ovary. (a) The right ovary is normal. (b) The left ovary shows a 6-cm mass with internal hemorrhage.



(a) (b)

Figure 2. Magnetic resonance image of the left adnexal region (→) and right ovary (→). (a) T1-weighted images show a heterogeneous mass with low to equal signaling. (b) T2-weighted images show a mixed mass with low and high signals suggestive of a hematoma.

Based on the clinical finding of lower abdominal pain, we suspected an intraovarian hematoma associated with torsion of the left ovarian tumor or the enlarged ovary due to ovarian bleeding. Regarding the secondary amenorrhea, the right ovary was mildly polycystic on transvaginal ultrasonography, and blood tests showed the following levels: LH, 16.9 mIU/mL; FSH, 3.0 mIU/mL; estradiol (E2), 27.7 pg/mL; progesterone (P4), 0.3 ng/mL; testosterone, 1.09 ng/mL; and AMH, 8.91 ng/mL. PCOS was diagnosed based on the high LH, tes-

tosterone, and AMH levels (Table 1). As the patient wanted to preserve her fertility, LOD was selected to treat the PCOS, and because the left ovary became enlarged again after shrinking, surgery was planned at the same time to check its condition.

Table 1. Tumor makers and hormonal assessment before and after surgery.

Tumor marker	Pre-surgery	Post-surgery
CEA (ng/ml)	1.3	1.4
CA19-9 (U/ml)	20.2	18.3
CA125 (U/ml)	8.4	13.3
Hormones		
LH (mlU/mL)	16.99	2.58
FSH (mlU/mL)	3.0	8.91
PRL (ng/ml)	8.71	
Estradiol (pg/mL)	27.7	97.0
Test (ng/ml)	1.09	0.17
AMH (ng/mL)	8.91	1.13
Progesterone (ng/mL)	0.30	0.16

The left ovary was 6 cm across and adherent to the mesentery, suggesting that the PCOS was complicated by an ovarian tumor. The tumor was fragile and retained its original morphological features. The tumor capsule was dissected, and the tumor was removed. Since the right ovary was grossly PCOS-like, LOD was performed (Figure 3(a), Figure 3(b)).

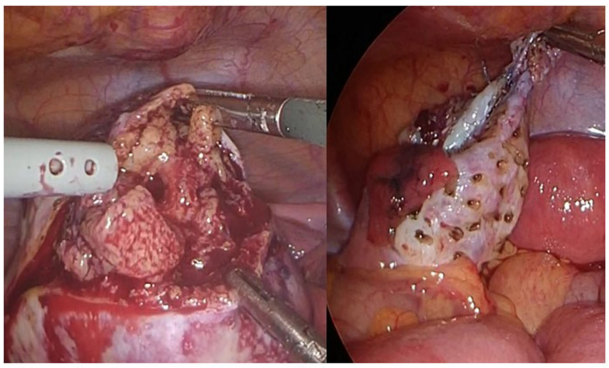


Figure 3. Laparoscopic surgical findings. (a) Cystectomy revealed that the left ovarian tumor was very fragile. (b) Drilling was performed on the right ovary.

A microscopic examination of the left ovarian tumor revealed coffee bean–like nuclei of atypical cells forming small and large island-like foci as well as proliferating cells. (Figure 4) Within the foci, organized cells or acidophilic materials are surrounded by atypical cells that form microfollicular structures called

Call–Exner bodies. The tumor cells were positive for calretinin, estrogen receptors, and progesterone receptors. Based on the histopathological examination, the diagnosis was AGCT of the left ovary.

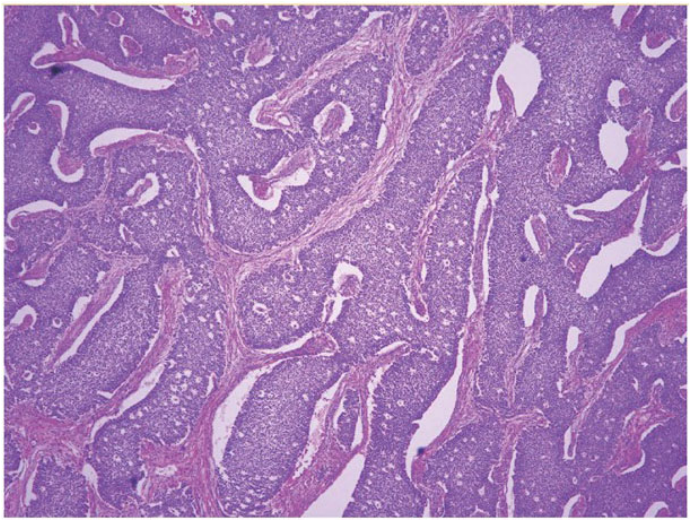


Figure 4. Histopathological findings of the lesion. The left ovarian tumor featured coffee bean-like nuclei of atypical cells forming small and large island-like foci as well as proliferating cells.

Blood tests performed at approximately 1 month postoperative showed the following levels: LH, 2.58 mIU/mL; FSH, 8.91 mIU/mL; E2, 97.0 pg/mL; P4, 0.16 ng/mL; testosterone, 0.17 ng/mL; AMH, 1.13 ng/mL; CA125, 13.3 U/mL; CA19-9, 18.3 U/mL; and carcinoembryonic antigen (CEA), 1.4 ng/mL. The LH, testosterone, and AMH levels were normal (**Table 1**). After we explained the future treatment regimen for GCT, the patient requested to receive treatment at a specialized oncology hospital. Because of her desire to preserve her fertility, she underwent an additional left adnexectomy, partial oophorectomy, and intraperitoneal exploration at another hospital. No obvious extraovarian lesions or residual tumors were observed at the resection site. The patient was ultimately diagnosed with stage I disease, for which no additional treatment was administered.

3. Discussion

PCOS has been the leading cause of anovulatory infertility in recent years, causing infertility in 70% - 80% of affected women [11]. High LH is among its characteristics [12]; elevated AMH also appears to be correlated [2]. Our patient presented with secondary amenorrhea and high LH, testosterone, and AMH levels, which led to the diagnosis of PCOS according to Rotterdam criteria (2003). Treatments for PCOS-related infertility include clomiphene citrate (CC), gonadotropin (Gn), LOD, and assisted reproductive technology. CC therapy, which plays a major role in inducing ovulation in women who wish to conceive [13], remains the first choice in women with PCOS [14]. Approximately 15% - 40% of patients are CC-resistant and require secondary Gn therapy [13]. However, Gn

therapy is associated with ovarian hyperstimulation syndrome (OHSS) and/or multiple pregnancies [14], which raises the need for in vitro fertilization (IVF) after CC without Gn therapy. However, not all women want to undergo IVF; thus, clinicians generally explore and choose methods other than IVF rather than proceeding with step-up treatment [15]. Therefore, we actively chose LOD in this case [11] [16], which is reportedly as effective as Gn therapy for women with anovulatory PCOS without carrying the risk of OHSS or multiple pregnancies [13] and may have a sustained effect that allows multiple pregnancies [16]. Decreased androgen and AMH levels have been observed [17], and spontaneous ovulation and CC responsiveness improve hyperandrogenemia and decrease AMH levels [13]. For patients undergoing infertility treatment, laparoscopic surgery enables the simultaneous diagnosis and treatment of intra-abdominal lesions without major invasion. Although several reports of concomitant PCOS and AGCT have been reported [4] [5] [18]-[21], only our patient underwent aggressive laparoscopic surgery. In this case, MRI showed no aggressive malignant findings (**Figure 2**), tumor markers were normal (**Table 1**), and the aggressive laparoscopic surgery was not problematic. Intraoperatively, an ovarian cystectomy performed to evaluate the left ovary revealed a tumor; however, the pathological result was AGCT.

GCT, like PCOS, can manifest as amenorrhea, and the abnormal proliferation of granulosa cells results in the excessive secretion of estrogen, inhibin, and AMH [4]. Its definitive diagnosis depends on pathological findings; however, MRI is also useful as a preoperative diagnostic imaging modality. GCT are typically multifocal cystic masses composed of small and large follicles with hemorrhagic contents, with high vascularity [22], and varying in size and density [23]. MRI shows a hemorrhage within an ovarian cystic mass that can be differentiated from ovarian hemorrhage as well as the presence of a hemorrhagic tumor or epithelial ovarian malignancy [24]. MRI in this case showed similar findings with clearly visible hemorrhage (**Figure 2**). However, the presence of lower abdominal pain strongly suggested ovarian torsion; therefore, we judged the bleeding as being due to torsion. Since the ovary subsequently shrunk, we did not suspect the presence of aggressive malignant changes.

In our review of surgeries for tumors in PCOS and AGCT, we identified several reports of concomitant conditions. In one case, no obvious evidence of an ovarian tumor was noted; however, bilateral oophorectomy was chosen to improve the patient's severe masculinizing signs [21]. Our patient's testosterone levels were also elevated, although not extremely (to 1.09 ng/mL), but she displayed no signs of masculinization. In another two cases, large tumors (>10 cm) were detected (16 cm and 19 cm), for which unilateral adnexectomy was performed [18] [20]. One relatively large tumor (8 cm) treated with unilateral adnexectomy after tumor resection because of suspected GCT on rapid pathology [19]. The other two cases were relatively small tumors (3.6 cm and 4.7 cm), for which tumor resection was initially selected [4] [5]. However, as all patients wished to preserve their fertility, they underwent additional staging surgery:

unilateral adnexectomy + partial omentectomy + intraperitoneal exploration. In this case, the tumor was not large, measuring 61.0 × 40.3 mm at the hospital visit, and shrinkage was noted afterward (**Figure 1**). Therefore, ovarian cystectomy was initially selected. After the pathological diagnosis was made, the patient wished to preserve her fertility, so a staging surgery was performed, after which no residual tumor was detected. In these five cases, the surgical technique was generally determined by tumor size. For relatively large ovarian tumors, size suggests malignancy [25] and an adnexectomy is performed. In cases of concomitant PCOS and GCT, a high LH level was found in four of five cases with measurements, a high AMH level in all three cases with measurements, and a high testosterone level in five of six cases. All three hormone levels were elevated in only the current case. Tumor markers CA125 and CA19-9 were measured in three and two patients, respectively, and all were within the normal range. The levels of both tumor markers were within the normal range in this case as well (**Table 1**).

AMH is produced by anterior and follicular follicles, while inhibin is produced by anterior follicles [4]. Women with PCOS have AMH levels that are 2 - 3 times higher than those in women without PCOS due to the increased number of anterior and follicular follicles [11]. Since this patient also showed elevated levels of LH, AMH, and testosterone but normal CEA, CA125, and CA19-9 levels (**Table 1**), we did not consider any causes other than PCOS. Furthermore, we did not consider the possibility of coexisting PCOS and GCT. However, we were aware that AMH and inhibin β are considered reliable and useful markers for GCT diagnosis and recurrence [6] and may present clinical findings similar to those of PCOS. In one reported case, inhibin β levels were measured postoperatively [4] and the values were in the normal range. In this case, we did not measure inhibin β due to lack of information at the time. GCT images are most easily obtained via transvaginal ultrasonography; however, sclerotic images have been described in several cases [4] [5] [18]. On ultrasonography, GCT may present as a hard cystic, multifocal [18], or hard mass with variable echogenicity, usually with a hemorrhagic component and vascular growth visible on color Doppler [5]. The ultrasound findings in the present case were not obviously cystic but rather a mass that was suggestive of a hematoma with a rather hard impression (**Figure 1**). However, ultrasound findings of GCT are reportedly indistinguishable from those of other ovarian neoplasms [19].

Fortunately, GCT are often stage I and localized to a single ovary [8] and feature 5-year survival rates at clinically advanced stages I and II of 98% and 84%, respectively [6]. The latest international guidelines state that the primary treatment for GCT is standard staging surgery [26]; however, several studies have reported that FSS (excision of the affected adnexa plus intraperitoneal exploration) does not affect recurrence or survival rates [7] [9] [10]. A stage I diagnosis allows preservation of the uterus and contralateral ovary as well as FSS for patients who wish to preserve their fertility [26]. The presence of a residual tumor or tumor rupture at the time of initial surgery is a poor prognostic factor [27], so

removing the tumor without incident is important. Although no residual tissue was noted in this case after the additional staging surgery, the choice of initial ovarian cystectomy requires careful consideration.

4. Conclusion

PCOS treated almost exclusively as a benign disease complicated by GCT is extremely rare. Counseling, including fertility preservation as a preoperative examination target, is very important [28], and a more detailed description of the impact of surgery is needed.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] March, W.A., Moore, V.M., Willson, K.J., Phillips, D.I.W., Norman, R.J. and Davies, M.J. (2009) The Prevalence of Polycystic Ovary Syndrome in a Community Sample Assessed under Contrasting Diagnostic Criteria. *Human Reproduction*, **25**, 544-551. https://doi.org/10.1093/humrep/dep399

[2] Dumont, A., Robin, G., Catteau-Jonard, S. and Dewailly, D. (2015) Role of Anti-Müllerian Hormone in Pathophysiology, Diagnosis and Treatment of Polycystic Ovary Syndrome: A Review. *Reproductive Biology and Endocrinology*, **13**, Article No. 137. https://doi.org/10.1186/s12958-015-0134-9

[3] Frandsen, C.L.B., Svendsen, P.F., Nøhr, B., Viuff, J.H., Maltesen, T., Kjær, S.K., *et al.* (2023) Risk of Epithelial Ovarian Tumors among Women with Polycystic Ovary Syndrome: A Nationwide Population-Based Cohort Study. *International Journal of Cancer*, **153**, 958-968. https://doi.org/10.1002/ijc.34574

[4] Triantafyllidou, O., Sigalos, G., Oikonomou, I. and Vlahos, N. (2018) Ovarian Granulosa Cell Tumor and Clomiphene Citrate Resistance. a Case Report and Review of the Literature. *JBRA Assisted Reproduction*, **22**, 381-384. https://doi.org/10.5935/1518-0557.20180056

[5] Kim, Y.S. and Lee, J.H. (2021) A Case Report of Ovarian Granulosa Cell Tumor in Patient with Polycystic Ovarian Syndrome. *Medicine*, **100**, e28261. https://doi.org/10.1097/md.0000000000028261

[6] Li, J., Chu, R., Chen, Z., Meng, J., Yao, S., Song, K., *et al.* (2021) Progress in the Management of Ovarian Granulosa Cell Tumor: A Review. *Acta Obstetricia et Gynecologica Scandinavica*, **100**, 1771-1778. https://doi.org/10.1111/aogs.14189

[7] Sun, H., Lin, H., Jao, M., Wang, K., Liou, W., Hung, Y., *et al.* (2012) A Long-Term Follow-Up Study of 176 Cases with Adult-Type Ovarian Granulosa Cell Tumors. *Gynecologic Oncology*, **124**, 244-249. https://doi.org/10.1016/j.ygyno.2011.10.015

[8] Schumer, S.T. and Cannistra, S.A. (2003) Granulosa Cell Tumor of the Ovary. *Journal of Clinical Oncology*, **21**, 1180-1189. https://doi.org/10.1200/jco.2003.10.019

[9] Wang, D., Cao, D., Jia, C., Huang, H., Yang, J., Wu, M., *et al.* (2018) Analysis of Oncologic and Reproductive Outcomes After Fertility-Sparing Surgery in Apparent Stage I Adult Ovarian Granulosa Cell Tumors. *Gynecologic Oncology*, **151**, 275-281. https://doi.org/10.1016/j.ygyno.2018.09.004

[10] Bryk, S., Färkkilä, A., Bützow, R., Leminen, A., Heikinheimo, M., Anttonen, M., *et al.* (2015) Clinical Characteristics and Survival of Patients with an Adult-Type Ovarian Granulosa Cell Tumor: A 56-Year Single-Center Experience. *International Journal of Gynecologic Cancer*, **25**, 33-41. https://doi.org/10.1097/igc.0000000000000304

[11] Collée, J., Mawet, M., Tebache, L., Nisolle, M. and Brichant, G. (2021) Polycystic Ovarian Syndrome and Infertility: Overview and Insights of the Putative Treatments. *Gynecological Endocrinology*, **37**, 869-874. https://doi.org/10.1080/09513590.2021.1958310

[12] Naz, R.K. (2014) Polycystic Ovary Syndrome Current Status and Future Perspective. *Frontiers in Bioscience*, **6**, 104-119. https://doi.org/10.2741/e695

[13] Mercorio, A., Della Corte, L., De Angelis, M.C., Buonfantino, C., Ronsini, C., Bifulco, G., *et al.* (2022) Ovarian Drilling: Back to the Future. *Medicina*, **58**, Article No. 1002. https://doi.org/10.3390/medicina58081002

[14] Lebbi, I., Ben Temime, R., Fadhlaoui, A. and Feki, A. (2015) Ovarian Drilling in PCOS: Is It Really Useful? *Frontiers in Surgery*, **2**, Article No. 30. https://doi.org/10.3389/fsurg.2015.00030

[15] Kawamura, M., Akiyama, M., Nakajima, R., Satoi, E., Ogaki, Y. and Kanda, R. (2024) Usefulness of Newly Devised Clomiphene Citrate Administration Method Compared with the Conventional Method in Ovulation and Pregnancy. *Open Journal of Obstetrics and Gynecology*, **14**, 637-649. https://doi.org/10.4236/ojog.2024.144055

[16] Debras, E., Fernandez, H., Neveu, M., Deffieux, X. and Capmas, P. (2019) Ovarian Drilling in Polycystic Ovary Syndrome: Long Term Pregnancy Rate. *European Journal of Obstetrics & Gynecology and Reproductive Biology: X*, **4**, Article ID: 100093. https://doi.org/10.1016/j.eurox.2019.100093

[17] Morley, L.C., Tang, T., Yasmin, E., Norman, R.J, and Balen, A.H. (2017) Insulin-Sensitising Drugs (Metformin, Rosiglitazone, Pioglitazone, D-Chiro-Inositol) for Women with Polycystic Ovary Syndrome, Oligo Amenorrhoea and Subfertility. *Cochrane Database of Systematic Reviews*, **11**, CD003053.

[18] Porestsky, L., Levesque, L., Seibel, M.M., Smith, D., Pazianos, A., Hurd, J., Aretz, T. and Flier, J. (1988) Characteristics of *in Vitro* Steroidogenesis in a Women with Hyoerandrogenesm, a Granulosa Cell Tumor and Polycystic Ovary Disease: A Case Report. *The Journal of Reproductive Medicine*, **33**, 377-381.

[19] Gu, C., Zeng, X., Shi, Q., Xiao, Q. and He, Y. (2022) Androgen-Secreting Adult Granulosa Cell Tumor in a Woman with Polycystic Ovary Syndrome: A Case Report. *Gynecological Endocrinology*, **38**, 1014-1016. https://doi.org/10.1080/09513590.2022.2143491

[20] Vera, L., Accornero, M., Mora, M., Valenzano-Menada, M., Minuto, F. and Giusti, M. (2013) Increasing Hirsutism Due to a Granulosa-Cell Tumor in a Woman with Polycystic Ovary Syndrome: Case Report and Review of the Literature. *Gynecological Endocrinology*, **29**, 273-277. https://doi.org/10.3109/09513590.2012.743012

[21] Harris, A.A. and Kabadi, U.M. (2020) More than Meets the Eye in a Patient with PCOS: Androgen-Secreting Granulosa Cell Ovarian Tumor in a Virilized Woman with Polycystic Ovarian Syndrome (PCOS). *AACE Clinical Case Reports*, **6**, e170-e173. https://doi.org/10.4158/accr-2019-0576

[22] Morikawa, K., Hatabu, H., Togashi, K., Kataoka, M.L., Mori, T. and Konishi, J. (1997) Granulosa Cell Tumor of the Ovary: MR Findings. *Journal of Computer Assisted Tomography*, **21**, 1001-1004. https://doi.org/10.1097/00004728-199711000-00028

[23] Kim, S.H. and Kim, S.H. (2002) Granulosa Cell Tumor of the Ovary: Common Findings and Unusual Appearances on CT and Mr. *Journal of Computer Assisted Tomography*, **26**, 756-761. https://doi.org/10.1097/00004728-200209000-00016

[24] Nyberg, D.A., Porter, B.A., Olds, M.O., Olson, D.O., Andersen, R. and Wesby, G.E. (1987) MR Imaging of Hemorrhagic Adnexal Masses. *Journal of Computer Assisted Tomography*, **11**, 664-669. https://doi.org/10.1097/00004728-198707000-00021

[25] Erkılınç, S., Taylan, E., Karataşlı, V., Uzaldı, İ., Karadeniz, T., Gökçü, M., *et al.* (2019) Does Lymphadenectomy Effect Postoperative Surgical Morbidity and Survival in Patients with Adult Granulosa Cell Tumor of Ovary? *Journal of Obstetrics and Gynaecology Research*, **45**, 1019-1025. https://doi.org/10.1111/jog.13928

[26] Ray-Coquard, I., Morice, P., Lorusso, D., Prat, J., Oaknin, A., Pautier, P., *et al.* (2018) Non-Epithelial Ovarian Cancer: ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. *Annals of Oncology*, **29**, iv1-iv18. https://doi.org/10.1093/annonc/mdy001

[27] Ebina, Y., Yamagami, W., Kobayashi, Y., Tabata, T., Kaneuchi, M., Nagase, S., *et al.* (2021) Clinicopathological Characteristics and Prognostic Factors of Ovarian Granulosa Cell Tumors: A JSGO-JSOG Joint Study. *Gynecologic Oncology*, **163**, 269-273. https://doi.org/10.1016/j.ygyno.2021.08.012

[28] Chelariu-Raicu, A., Cobb, L.P. and Gershenson, D.M. (2021) Fertility Preservation in Rare Ovarian Tumors. *International Journal of Gynecologic Cancer*, **31**, 432-441. https://doi.org/10.1136/ijgc-2020-001775