CASE REPORT PEER REVIEWED | OPEN ACCESS

Treat secondary amenorrhea by oophorectomy: A case of adult granulosa cell tumor with pseudo-FSH deficiency manifested by secondary amenorrhea

Hoo PS, Nik Rafiza Afendi, Lou Wei Yeng, Ahmad Shuib Yahaya, Ahmad Amir Ismail, Rahimah Abdul Rahim, Ahmad Akram Omar, Mohd Pazudin Ismail

ABSTRACT

Introduction: Granulosa cell tumor of the ovary is a very rare cancer, accounting for only 0.6–3% of all ovarian tumors. Histologically, it belongs to the category of sex-cord stromal tumors, comprising 70% of tumors of this group. Commonly, the tumors secrete oestrogen, so the patients usually presented with precocious puberty, menorrhagia, metrorrhagia or post-menopausal bleed. Case Report: We report a case of adult granulosa cell tumor of right ovary with atypical presentation. The patient presented to us with secondary amenorrhea. Ultrasound scan showed mixed solid cystic right adnexal mass measuring 6.7x9.5x8.7 cm. The preoperative hormonal profiles showed suppressed follicle stimulating hormone (FSH) 0.2 IU/L, normal luteinizing hormone 8.1 IU/L, elevated estradiol 650.1 pmol/L and testosterone 2.5 nmol/L but no sign of virilization. Laparotomy salpingo-oophorectomy and omentectomy was electively performed and she regains her menses and her hormonal profiles were normalized one month later. The histopathology reported as adult granulosa cell tumor stage 1A. She is still under our outpatient follow-up. Conclusion: Sudden onset of secondary amenorrhea with ovarian tumor should raise high suspicion of hormonal secreting tumor.

Keywords: Granulosa cell tumor, Secondary amenorrhea, Sex-cord stromal tumor

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INTRODUCTION

Ovarian granulosa cell tumor is a very rare type of ovarian tumor, accounting for only 0.6–3% of all ovarian tumors [1]. Histologically, it belongs to the category of sex-cord stromal tumors, comprising 70% of tumors of

this group. Commonly, the tumors secrete oestrogen, which contributes to precocious puberty, menorrhagia, metrorrhagia or postmenopausal bleeding. We report a case of atypical presentation of ovarian granulosa cell tumor presented with secondary amenorrhea associated with elevated estradiol and testosterone with suppressed follicle stimulating hormone (FSH).

CASE REPORT

We report a 42-year-old female, para 7+2 abortions, presented with amenorrhea for 14 months. Her last child birth was 3 years ago. Her previous menstrual cycle was regular and she was not on hormonal contraception. Upon further history, she noticed suprapubic mass since one year ago, with intermittent abdominal discomfort for the past three months. There was no obstructive symptom or changes in bowel or urinary habits. There was no abnormal per vaginal discharge. She denied loss of weight or appetite, dyspareunia or post-coital bleeding. Last year cervical smear was normal.

Per abdomen examination revealed well rounded, firm suprapubic mass measuring 8x8 cm, smooth surface, regular margin and freely mobile. There was no ascites or hepatosplenomegaly.

Ultrasound scan showed right adnexal mass, mixed solid and cystic in consistency with predominantly solid component, measuring 9x8x6 cm. There was no papillary projection and no color Doppler uptake. Uterus was 9x4 cm. Endometrium thickness 3.8 mm. There was no ascites, liver and both kidneys appeared normal.

Computed tomography (CT) scan showed oval shaped, mixed solid and cystic (predominantly solid) right adnexal mass measuring 6.7x9.5x8.7 cm. The solid component heterogeneously enhanced in post contrast images while the cystic components are multiloculated with thick enhancing septae. There were no significant enlarged pelvic nodes or ascites.

All tumor markers were in normal range. The endocrinology evaluation revealed a suppressed follicle stimulating hormone (FSH) 0.2 IU/L, normal luteinizing hormone 8.1 IU/L, elevated estradiol 650.1 pmol/L and testosterone 2.5 nmol/L. Serum prolactin was normal 99.2 miu/L. Inhibin test was unavailable

Exploratory laparotomy was performed. Intraoperatively there was minimal straw color intra-peritoneal fluid and sent for cytology. Right ovarian tumor measuring 12x8 cm, mixed solid and cystic in consistency with intact capsule. Right salpingo-oophorectomy and omentectomy were done. The left fallopian tube, ovary and uterus appeared normal. The peritoneum, omentum and liver were unremarkable.

Histopathological examination reported as adult granulosa cell tumor of the right ovary with no tumor deposits seen in right fallopian tube and omentum.

The patient recovered well after the operation and regain menstruation one month postoperation. Repeated hormonal profiles were within normal range. The result is given in Table 1. Currently, she is under our surveillance every six month at gynecology clinic.

DISCUSSION

Granulosa cell tumor is a very rare tumor, accounting for only 0.6–3% of all ovarian tumors [1]. Previously, these tumors typically produce oestrogens and therefore abnormal vaginal bleeding is the norm. However, there are some cases that presented with secondary amenorrhea too [2, 3]. In these cases, we found that most of the hormonal profiles were deranged and associated with raised Inhibin, causing the low FSH level and therefore a state of pseudo-FSH deficiency [4].

Our case was differ from the others with the estradiol level markedly elevated instead of low or normal [2, 5, 6]. So far there was no report that presented with secondary amenorrhea yet with such elevated oestrogens and pseudo FSH deficiency with normal luteinizing hormone. Most of the cases reported that after removal of the tumor, menses resume and the hormonal profile back to normal. The comparison is given in Table 2.

The pathophysiology of pseudo-FSH deficiency was related to elevated inhibin level, which has the ability to specifically suppress the FSH secretion from pituitary cells in vitro [7]. During early follicular phase, the elevated FSH promote development of follicles and therefore increasing inhibin level. The inhibin was secreted by the granulosa cells of preantral, antral and

Table 1: Change of hormones

	Preoperative	One month after surgery
Follicle stimulating hormone (IU/L)	0.2	9.2
Luteinizing hormone (IU/L)	8.1	3.7
Estradiol (pmol/L)	650.1	158.4
Testosterone (nmol/ L)	2.5	0.4

Table 2: Hormonal profile of literature reviews

Authors	Age	LH (IU/L)	FSH (IU/L)	Estradiol (pmol/L)
Krishnan et al. [5]	36	6.7	0.8	129
Kurihara et al. [3]	31	9.8	0.3	142
Agha-Hosseini et al. [6]	26	1.4	0.1	100
Decoudier et al. [4]	41	2.1	0.2	156
Our case	42	8.1	0.2	650

LH: Luteinizing Hormone
FSH: Follicle Stimulating Hormone

large antral follicles which in normal condition will give negative feedback to the FSH during day-5 to day-9 of menstrual cycle. Follicle stimulating hormone level start to fall and the subsequently enlarging dominant follicle will response to the luteinizing hormone luteinization occur, will fall of inhibin level. However in granulosa cell tumor, the production of inhibin is unaffected by FSH, resulting in marked suppression of FSH. The estradiol in this patient is markedly elevated but surprisingly there was no frequent irregular bleeding or endometrial hyperplasia as reported in other literatures [8–10].

In true FSH deficiency as pointed out by Krishnan et al. [5], usually presented as primary amenorrhea characterised by absent to low FSH, low levels of estradiol, and normal luteinizing hormone such as in cases of mutation of FSH beta gene. In pseudo-FSH deficiency however, the isolated suppression of FSH by inhibin will be manifested as low FSH and normal luteinizing hormone.

This case is a atypical presentation of ovarian granulosa cell tumor presented with secondary amenorrhea associated with elevated estradiol and testosterone with suppressed follicle stimulating hormone.

CONCLUSION

In conclusion, clinicians should have high index of suspicion whenever encounter patient with sudden onset secondary amenorrhea or early menopause especially with concomitant ovarian tumor.

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Author Contributions

Hoo PS – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published.
Nik Rafiza Afendi – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Lou Wei Yeng – Substantial contributions to conception and design, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published
Ahmad Shuib Yahaya – Substantial contributions to conception and design, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published
Ahmad Amir Ismail – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published.
Rahimah Abdul Rahim – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published.
Ahmad Akram Omar – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published.
Mohd Pazudin Ismail – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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