Case Report

DOI: 10.7860/JCDR/2013/6911.3507

Delayed Menopause Due to Ovarian Granulosa Cell Tumour

Obstetrics and Gynaecology Section

NEETHA VYAS M.[1], LAKSHMI MANJEERA[2], SUPRIYA RAI[3]

ABSTRACT

A patient presented to us with complaints of inability to attain menopause even at the age of 64. She has been having irregular cycles of bleeding for 5 days every 2-3 months from the age of 54. On evaluation, she was found to have endometrial hyperplasia and ultrasonography showed a homogenous solid ovarian mass of size of the 4 cm x 3.5 cm. She underwent staging laparotomy with total abdominal hysterectomy bilateral salpingo-oophorectomy and infra colic omentectomy. Histopathology confirmed granulosa cell tumour of the ovary. Most commonly granulosa cell tumour presented with post–menopausal bleeding and abnormal uterine bleeding, however, women with delayed menopause also have to be evaluated thoroughly for estrogen secreting ovarian tumours. There should be an element of suspicion if patient doesn't attain menopause as specified and they need to be evaluated in detail.

Key words: Delayed menopause, Granulosa cell tumour, Ovarian tumor

INTRODUCTION

The average age of menopause is 51 years. It is genetically determined. But certain factors like smoking, high altitude and thin built accelerate menopause [1]. The age of menopause is independent of socio-economic state, race and nutritional status. One of the rare causes of late menopause is Granulosa Cell Tumour (GCT) of the ovary. Two-third GCT patients present with endocrine syndromes due functional tumors [2]. It may present with various presentations like precocious puberty, abnormal uterine bleeding (AUB), pelvic pain, pelvic mass or can remain asymptomatic. One of the rare but possible presentations of GCT is delayed menopause. Here, we present a 64–year–old lady who came to us with the complaint of inability to attain menopause.

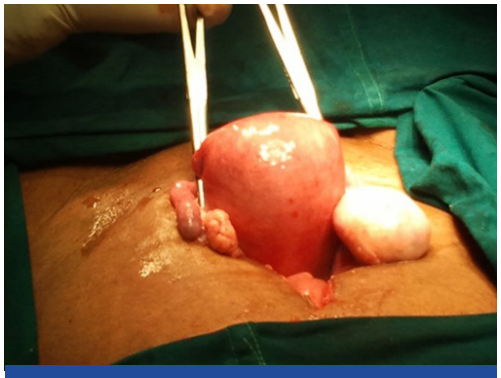
CASE REPORT

A 64–year–old parous lady presented to us with the complaint of inability to attain menopause. She had regular cycles till the age of 54. Since last 10 years, her cycles were irregular, with bleeding for four days every 2 to 3 months. She had undergone endometrial biopsy in some other hospital. Histopathology report revealed simple hyperplasia without atypia. Abdominal and speculum examination were unremarkable. Bimanual examination showed uterus enlarged (size at 10 weeks) with multiple small fibroids and a right adnexal mass.

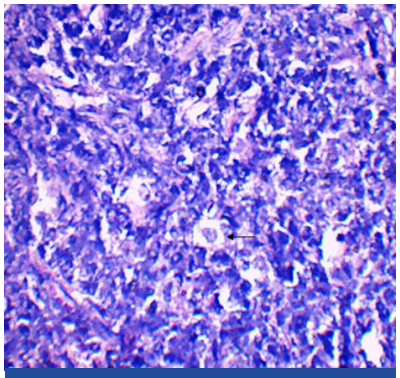
Ultrasound showed uterus bulky with small fibroids. Endometrial thickness was 8 mm. Right ovary showed a 4x3.5 cm homogenous solid mass. Left ovary was normal. No evidence of ascites or enlarged lymph nodes. Ca-125 level was normal. Contrast computed tomography and other tumor markers were advised for complete work up but due to financial constraints patient was not willing to do the investigations.

A staging laparotomy was done. There was no ascites intra–operatively. Saline washings were collected for cytology. Uterus appeared mildly enlarged with multiple small fibroids. Right ovary was enlarged about 5x3 cm in size, solid in appearance [Table/Fig-1]. Left ovary appeared normal. No peritoneal or omental deposits were noted. Systematic palpation of all abdominal organs revealed no deposits. Total abdominal hysterectomy with bilateral salphingoophrectomy and infracolic omntectomy was done. No lymph nodes were enlarged. Frozen section facilities were not available.

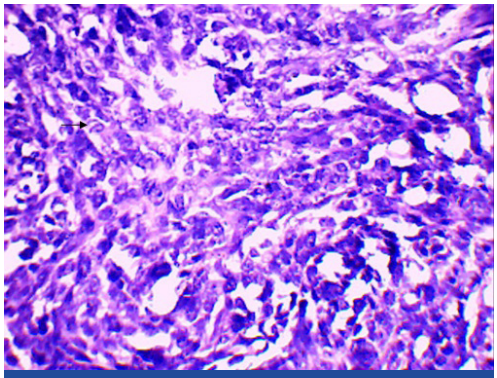
Grossly on histopathology, uterus was 11x3.5 cm with multiple fibroids of 1.5x1cm in size. Right ovary was 5x3.5cm size and on cut section, it appeared as a homogenous solid tumour with yellow and white areas. Left ovary was normal. Microscopy showed granulosa cells in sheets with call exner bodies [Table/Fig-2] and typical coffee bean appearance of nucleus [Table/Fig-3] confirming the diagnosis of granulosa cell tumour. Peritoneal washings showed no malignant cells. So a case of stage IA granulosa cell tumor was confirmed. Patient recovered well after the procedure and was advised to come for follow up.



[Table/Fig-1]: Right side solid ovarian mass



[Table/Fig-2]: Histology of granulosa cell tumour showing microfollicular pattern with typical call exner bodies (arrow)



[Table/Fig-3]: Showing granulosa cells with nuclear grooving giving a coffee–bean appearance (arrow)

DISCUSSION

Granulosa cell tumour of the ovary is a rare neoplasm accounting for approximately 1.5-3% of all ovarian tumours [1]. It belongs to sex cord stromal tumours. There are two types. They can be adult type which accounts to 95% of all GCTs and juvenile type which is 5% of all GCTs. Adult GCT occurs more often in post–menopausal women with a peak incidence between 50-55 years of age. This tumour produces estrogen, reason for an early diagnosis. About 70% of tumours are hormone secreting [2]. Symptoms depending on the age and type of secretion, pre–puberty girls may experience isosexual precocious puberty caused by hyperestrogenism. The most common presentation in peri–menopausal and menopausal age group is abnormal uterine bleeding (53.7%). Either it could present as postmenopausal bleeding (27.5%), heavy or irregular menstruation (26.2%), or amenorrhoea [3]. Other symptoms include abdominal or pelvic pain, abdominal mass and abdominal distension. Adult GCT can also present with virilising symptoms when androgen production is in excess. Interestingly, in our case patient presented for inability to attain menopause which is quite rare but possible way of presentation. None of the clinico-pathological studies regarding GCT have noted or given any significance to patients presenting with delayed menopause. In fact, in a case which was reported as delayed menopause at age of 52, the ovaries appeared grossly normal [1]. Only on histopathological examination a diagnosis of GCT was done. Around 23% of patients remain asymptomatic [4]. Around 50% of patients develop endometrial hyperplasia and another 8-33% has associated endometrial adenocarcinoma [5]. O Ukah et al., reported a case adult GCT with endometrial carcinoma where they mentioned association of endometrial adenocarcinoma with GCT has < 5% and most of the cancers were well differentiated [6].

It has been highlighted that women with AUB have to be thoroughly evaluated by imaging techniques for estrogen secreting ovarian tumours. On ultrasound, GCT appears round to ovoid masses that are multi–cystic with solid components. Fewer cases can appear as homogenous solid masses.

Inhibin is used as a tumor marker for GCT. Inhibin is a peptide hormone produced by ovarian granulosa cells. In a study by Robertson et al., [7], total serum inhibin level was elevated in 100% GCTs, although, Inhibin A and B levels are elevated in patients with GCT, Inhibin B levels are usually elevated in higher proportion of tumours. Mom et al., [8] evaluated the use of serum inhibin levels in 30 women with granulosa cell tumours. The sensitivities and specificities for inhibin A were 67% and 100% and for inhibin B were 89% and 100%, respectively. Serum Inhibin levels are used for long term follow up of patients with lead time from elevation of inhibin to clinical recurrence being 11 months.

GCTs are tumours of low–malignancy potential. GCTs are staged surgically according to FIGO classification. Characterised by good prognosis and early detection early. Around 90% are at stage I during diagnosis. The high detection rate at an early stage is due to endocrine symptoms caused by functioning tumors. Stage of the tumors is the most important prognostic factor predicting recurrence, additional studies about age, menopausal status, post-op residual lesion and positive cytology washings are required [9]. Low staging at diagnosis confers an excellent prognosis with a 5 year survival rate of 75-95% (Stage 1) and survival rate drops down with advanced stage [10]. Though the prognosis of granulosa cell tumours is good, patients have to be on long term follow up to detect late recurrence. Surveillance is done by frequent examination and assessment of tumour markers. Currently Anti–Mullerian Hormone (AMH) has been found to be more specific for GCT [11]. It has a sensitivity of 76% and a specificity of 93% and can be used as a prognostic marker [11].

To conclude, GCTs can have various presentations depending on age and hormone secretion. Patients can have endocrine symptoms that often present early in these functioning tumours. One of rare symptom or way of presentation of GCTs could be delayed menopause. This case is being reported to highlight not to ignore cases of delayed menopause. One needs to be vigilant and such cases need thoroughly evaluation to rule out estrogen secreting tumours.

REFERENCES

[1] Murkey B, Nadkarni T, Bhalerao S, Jassawalla MJ. Delayed menopause due to granulosa cell tumor of the ovary. *J Mid-life Health.* 2011; 2: 86-88.
[2] KD.Crew, MH.Cohen, DH Smith, AD Tiersten, NM Feirt, DL Hershman. Long natural history of recurrent granulosa cell tumor of ovary 23years after initial diagnosis: a case report and review of literature. *Gynecol Oncol.* 2005; 96:235-40.
[3] A Ayhan, MC Slman, M Velipasaoglu, M Sakinci, K Yuce. Prognostic factors in adult granulosa cell tumors of the ovary: a retrospective analysis of 80 cases. *J Gynecol Oncol.* 2009; 20:158-63.
[4] D Pectasides, G Papaxoinis, G Fountzilas, G Aravantinos, E Pectasides, D Economopoulos et al. Adult granulosa cell tumors of the ovary: A clinicopathological study of 34 patients by the Hellenic Cooperative Oncology Group (HeCOG). *Anticancer research.* 2008; 28:1421-28.
[5] You XL, Yin RT, Li KM, Wang DQ, Li L, Yang KX. Clinical and pathological analysis on ovarian granulosa cell tumors. *Sichuan Da Xue Xue Bao Yi Xue Ban.* 2010; 41: 467-70.
[6] Cornelius O Ukah, Okechukwu C Ikpeze, George U Eleje, Ahizechukwu C Eke. Adult granulosa cell tumor associated with endometrial carcinoma: a case report. *Journal of medical case reports.* 2011; 5:340.
[7] Robertson DM, Stephenson T, Pruysers E. Characterization of inhibin forms and their measurement by an inhibin alpha-subunit ELISA in serum from postmenopausal women with ovarian cancer. *J Clin Endocrinol Metab.* 2002; 2: 816-24.
[8] Mom CH, Engelen MJ, Willemse PH, Gietema JA, Ten Hoor KA, De Vries EG, et al. Granulosa cell tumors of the ovary: The clinical value of serum inhibin A and B levels in a large single center cohort. *Gynecol Oncol.* 2007; 105: 365-72.
[9] In Ho Lee, Chel Hun Choi, Dae Gy Hong, Jae Yun Song, Young Jae Kim, Kyung Tai Kim et al. Clinicopathologic characteristics of granulosa cell tumors of the ovary: a multicenter retrospective study. *J Gynecol Oncol.* 2011; 22: 188-95.
[10] S Ali, P Gattuso, A Howard, MB Mosunjac, MT Siddiqui. Adult granulosa cell tumor: fine needle aspiration cytology of 10cases and review of literature. *Diagn Cytopathol.* 2008; 36:297-302.
[11] Korach J, Perri T, Beiner M, Davidzon T, Fridman E, BenBaruch G. Promising effect of aromatase inhibitors on recurrent granulosa cell tumors. *Int J Gynecol Cancer.* 2009; 19: 830-33.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Obstetrics and Gynaecology, K.S. Hegde Medical Academy, Nitte University, Deralakatte, Mangalore, India.
2. Associate Professor, Department of Obstetrics and Gynaecology, K.S. Hegde Medical Academy, Nitte University, Deralakatte, Mangalore, India.
3. Professor, Department of Obstetrics and Gynaecology, K.S. Hegde Medical Academy, Nitte University, Deralakatte, Mangalore, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Neetha Vyas M.,
Assistant professor, Department of Obstetrics and Gynaecology,
K.S.Hegde Medical Academy, Nitte University, Deralakatte, Mangalore, India.
Phone: +91 9900001287, E-mail: nvyas_21@yahoo.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jul 11, 2013**
Date of Peer Review: **Aug 19, 2013**
Date of Acceptance: **Sep 01, 2013**
Date of Publishing: **Oct 05, 2013**