CASE REPORT

Large functional benign endometroid cystadenofibroma of the ovary leading to endometrial cystic glandular hyperplasia and postmenopausal bleeding

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SUMMARY

Benign endometroid cystadenofibroma of the ovary is a rare tumour with few reported cases. The association of endometroid cystadenofibroma with endometrial cystic glandular hyperplasia has not been previously reported to authors' knowledge. We are reporting a 75-year-old postmenopausal woman who presented with a large abdominopelvic mass corresponding to 30 weeks size gravid uterus and postmenopausal bleeding. She has a well-oestrogenised vagina. Ultrasound pelvis revealed a large cystic mass extending from pelvis to epigastrium with no solid component and few incomplete septations and no internal echoes. MRI findings showed mainly cystic component with few moderately enhancing, fine, incomplete septa. Endometrial aspiration reported histopathology of cystic glandular hyperplasia without atypia. Serum oestrogen level reported to be high (210 pg/mL). Hysterectomy with bilateral salpingo-oophorectomy was performed. Histopathology of the specimen revealed benign endometroid cystadenofibroma. She remained asymptomatic and disease free during her 6-month follow-up.

BACKGROUND

Benign endometroid cystadenofibroma of the ovary is a rare tumour with few reported cases. The exact incidence is not known but ovarian cystadenofibromas account for 0.1% of all ovarian neoplasm. There is presence of endometroid element in 15–35% cases with 60% of them being benign and rest being malignant.¹ Endometroid type is a histological variant of cystadenofibroma; others being serous, mucinous, clear cell and mixed types.^{2,3} Various ovarian tumours have been associated with elevated oestrogen levels in postmenopausal women leading to postmenopausal bleeding but these are mostly granulosa and theca cell tumours and occurrence of oestrogen-secreting epithelial tumours is exceedingly rare. The association of endometroid cystadenofibroma with endometrial cystic glandular hyperplasia has not been previously reported to the authors' knowledge. We are reporting this rare association in a postmenopausal woman leading to postmenopausal bleeding.

CASE PRESENTATION

A 75-year-old P₅L₅ postmenopausal woman presented to gynaecology clinic with bleeding per vaginum since 3 months and a lump in the lower

abdomen was noticed 6 months back. She was postmenopausal for 20 years and had no history of postmenopausal bleeding. She had history of pulmonary Koch's for which she received antitubercular therapy 10 years back. General physical examination was unremarkable. Abdominal examination revealed a large, mobile, non-tender, cystic mass arising from the pelvis and corresponding to 30 weeks sized gravid uterus. Gynaecological examination revealed a well-oestrogenised vagina inconsistent with her postmenopausal state. Pelvic examination revealed same mass felt high up along with retroverted normal sized uterus.

INVESTIGATIONS

Routine blood investigations were normal except for mild anaemia with haemoglobin of 9 g%. Chest x-ray showed normal findings. Ultrasound pelvis revealed a large cystic mass extending from pelvis to epigastrium with no solid component and few incomplete septations and no internal echoes. The mass seemed to be of ovarian origin. Uterus was normal in size with endometrial thickness of 18 mm. Doppler sonography revealed minimal vascularisation of the tumour in periphery with high blood flow impedance. Abdominal ultrasound had normal findings with no lymphadenopathy. MRI findings showed mainly cystic component with few moderately enhancing, fine, incomplete septa. Endometrial aspiration was performed with the reported histopathology of cystic glandular hyperplasia without atypia. Serum CA-125 level was 22.4 U/mL. Considering granulosa cell tumour as one of the probable diagnosis, we got serum inhibin B levels determined, which were within normal range for postmenopausal range (9.2 ng/L). The patient had a well oestrogenised vagina along with endometrial hyperplasia which is indicative of high oestrogen levels therefore the serum oestradiol level was determined and found to be high (210 pg/mL).

DIFFERENTIAL DIAGNOSIS

Granulosa cell tumour or theca cell tumour was the first differential diagnosis we thought of, owing to oestrogenising effect of the tumour. We got serum inhibin B determined as it is considered to be a sensitive marker for granulosa cell tumour but this marker was not found to be raised in our patient. Metastatic tumours and rarely epithelial tumours are associated with oestrogen excretion but

To cite: Singh N, Tripathi R, Mala YM, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-010323

association with endometrial hyperplasia is very rare. Considering the ultrasound report, many benign ovarian tumours like serous or mucinous cystadenomas can be considered as a differential diagnosis.

TREATMENT

The patient was scheduled for laparotomy. Further action was to be decided after histopathology of the frozen section specimen. Operative findings revealed small amount of free peritoneal fluid and a large, thin-walled, cystic mass filled with clear, serous fluid and filling almost entire abdominal cavity arising from right ovary. There was presence of few fine septations without any solid areas in the tumour. Uterus, left ovary and bilateral fallopian tubes were normal. Suction from the cystic mass was performed to reduce the size of tumour for extraction from abdominal cavity (figure 1). Tumour was sent for frozen section analysis which reported benign ovarian epithelial tumour. Other abdominal organs were palpated which seemed normal with no palpable lymph nodes. Hysterectomy with bilateral salpingo-oophorectomy was performed. Histopathology of the specimen revealed benign endometrioid cystadenofibroma (figure 2). The endometrium showed cystic glandular hyperplasia as reported earlier in endometrial aspiration biopsy (figure 3). Rest of the uterus and remaining adnexal structures showed unremarkable histopathology.

OUTCOME AND FOLLOW-UP

The patient remained asymptomatic during her postoperative period and was discharged on the eighth postoperative day. She remained asymptomatic and disease free during her 6 month follow-up. We got her serum oestradiol level determined at 6 months after surgery for academic interest and it was 20 pg/mL (normal limits for age).

DISCUSSION

Benign endometrioid cystadenoma is a rare benign epithelial ovarian tumour. It is usually reported in older and postmenopausal women but its occurrence in girls even as young as

Figure 2 Showing histopathological features of benign endometrioid cystadenofibroma. Long tubular endometrial type glands lined by tall columnar cells surrounded by swirls of long-spindled fibroblastic cells are seen.

17 years has been reported.⁴ These tumours are bilateral in 15% of cases.³ The most common presenting symptom is abdominal pain.⁵ Abnormal vaginal bleeding has been reported in few cases of cystadenofibromas.⁵⁻⁶ Our patient presented with postmenopausal bleeding and lump in abdomen.

Ovarian cystadenofibroma is an uncommon tumour in which fibrous stromal element constitutes the dominant component. Some authors believe cystadenofibromas to be a variant of cystadenomas with increased fibrous element but WHO listed them as a distinct subcategory of epithelial ovarian tumours in 1973.¹ These neoplasms originate from the surface epithelium and the underlying cortical connective tissue of the ovary, and belong to the group of tumours of Mullerian derivation.⁷ They constitute around 1.7% of all benign ovarian tumours.⁸ These tumours are usually benign. The degree of epithelial proliferation and its relation to the stromal component can classify the tumour as benign, borderline or malignant. The histological subtypes may include serous, mucinous, clear cell, endometrioid and mixed types. Endometrioid type mainly shows benign stromal

Figure 1 Showing gross picture of the specimen showing a large cystic ovarian tumour. Suction of the cystic fluid was performed without spillage to facilitate removal from the abdominal cavity.

Figure 3 Showing histopathology of endometrial biopsy specimen suggestive of cystic glandular hyperplasia. Endometrial biopsy showing tubular and cystically dilated glands dispersed in a compact stroma.

component with scattered foci of endometrioid glandular epithelia and the benign or malignant nature of tumour depends on cellular grade of endometrioid epithelia.⁹

Cystadenofibromas are predominantly cystic (solitary or multicystic) on ultrasound. Septations are seen in 30% cases and solid nodules or projections in 50% cases. The tumour is avascular in 50% cases whereas increased vascularity can be found in 50% cases with typical pattern of peripheral vascularisation with high blood flow impedance.¹⁰ Because of the solid component or irregular thick septae seen on ultrasound, even the benign tumour can be misdiagnosed as malignant on preoperative imaging. Cho *et al*² reported 32 cases of ovarian cystadenofibromas, of which 16 tumours were purely cystic and the remaining 16 were complex cystic on CT or MRI. The ones which showed complex, solid-cystic lesions were misdiagnosed as malignant tumours but later histology showed benign cystadenofibromas.

MRI is considered the preferred modality for imaging of complex ovarian masses. Outwater *et al*¹¹ described the MRI feature of cystadenofibroma, reporting it as low-signal intensity in T2W images owing to solid fibrous component of this tumour. Other features that have been reported are multiple high-T2-signal intensity areas associated with a low-signal intensity solid fibrous component, giving a sponge-like appearance and multicystic foci with thickened septae, demonstrating low-T2-signal intensity corresponding to its fibrous nature.¹² Unlike these findings, our patient had mainly cystic component with few moderately enhancing, fine, incomplete septa.

Though, in our patient, the gross appearance of tumour seemed to be like a benign one but, at times, these tumours may resemble malignant tumours grossly.^{2–8} Hence, frozen section may be useful in preventing unnecessary extensive surgical procedure. In most of the reported cases, staging laparotomy with hysterectomy and bilateral salpingo-oophorectomy has been performed.^{8–9} In premenopausal women, conservative surgery can be performed if frozen section report shows benign nature of tumour. In perimenopausal and postmenopausal women, total abdominal hysterectomy with bilateral salpingo-oophorectomy seems logical as some elements of malignancy may be reported in histopathology later. Our patient was postmenopausal woman and we performed pan-hysterectomy, as she also had endometrial hyperplasia.

Epithelial tumours are rarely reported to be functional but a study by Rome *et al*¹³ on functional ovarian tumours showed that oestrogen secretion was higher than normal in 50% benign and malignant epithelial tumours of the ovary. High oestrogen excretion was noted in 70% of patients with mucinous tumours and 4% of patients with serous tumours ($p < 0.001$).¹³ The study also reported evidence of oestrogen activity in the endometrium in these oestrogen secreting tumours but correlation between endometrial histology and oestrogen secretion was not seen. The association of cystadenofibromas with endometrial hyperplasia is quite uncommon. In a study spanning over 13 years, Czernobilsky *et al*⁶ compared 34 patients of cystadenofibroma with 39 patients of cystadenoma. None of the patients in this series had a histopathology of endometrioid type cystadenofibroma. Only one patient in cystadenofibroma group presented with vaginal bleeding and the endometrium in this case was inactive, whereas in patients with cystadenoma,

18% had cystic or adenomatous endometrial hyperplasia. There are some other case reports of cystadenofibromas having endocrine effects leading to endometrial proliferation but others doubt such endocrine activity.^{5–14} In our patient, there was definite oestrogen secretion leading to endometrial hyperplasia.

Learning points

- ▶ Benign endometrioid cystadenofibromas are rare epithelial tumours which usually present in women of age groups 45–65 years but may occur in younger patients too.
- ▶ They may be associated with oestrogen secretion and lead to abnormal uterine bleeding and postmenopausal bleeding, hence should be considered as a possible differential diagnosis in patients with ovarian mass with abnormal uterine bleeding.
- ▶ Oestrogenisation leading to endometrial hyperplasia may also be associated with this tumour.
- ▶ Frozen section should be taken to prevent extensive surgery as the tumour may masquerade as malignant tumour both on imaging and on gross examination.

Contributors NS has prepared the manuscript. The co-authors proof read the script. All the authors contributed in managing the patient.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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