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Postmenopausal endometriosis

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SUMMARY

A postmenopausal woman, in her 60s, married with no history of pregnancy, presented to our facility with an abdominal mass of 2 months duration that progressively increased in size. Physical examination revealed a mobile abdominal cystic mass measuring approximately 20×20×10 cm, accompanied by ascites. Transvaginal ultrasonography showed a hypoechoic cystic mass measured >14.6×12.5 x13.5×11.49 cm, with septa and papillary projections, and the Doppler colour score was +2, along with ascites. Based on the IOTA Simple Rules, this mass would be classified as malignant, because it meets the criteria for M2 (ascites) and M4 (irregular multilocular solid tumour ≥100 mm) features. Because malignancy was suspected, a total hysterectomy and bilateral salpingo-oophorectomy with a frozen section were performed. The frozen section and histopathological examination resulted in a right endometrioma. Postmenopausal endometriosis is rare, but clinicians should always be aware of its existence as it confers a risk of malignant transformation and recurrence. Comprehensive follow-up after surgery is recommended in such cases.

BACKGROUND

Endometriosis is a condition in which functioning endometrial glands and stroma are present outside the uterine cavity.[1] It is an oestrogen-dependent disease that commonly occurs in reproductive age women. Due to its nature, endometriosis has been linked with the occurrence of menstrual cycles. Nonetheless, it can afflict around 2–5% of postmenopausal women and is typically a side effect of hormonal therapy, particularly unopposed oestrogen use. The presence of endometriosis in postmenopausal women not receiving hormonal therapy underlines the complex mechanism of this condition.[2–4] In clinical practice, differentiating endometriosis from malignancies is essential. However, certain risk factors for endometriosis and ovarian cancer, such as low parity, infertility, late childbearing age and oral contraceptive use may overlap, making diagnosis more challenging.[5 6] Visual inspection through laparoscopy, preferably with histological confirmation, remains the gold standard for diagnosing endometriosis. Surgery is the primary treatment for endometriosis.[4] In this case report, we present a rare case of endometriosis in a postmenopausal woman in her 60s, without previous hormonal therapy that was initially suspected as ovarian cancer. We also review current literature on this rare condition.

CASE PRESENTATION

A postmenopausal woman, in her 60s, categorised as obese (weighing 59 kg and 150 cm tall), with no history of pregnancy, presented to our facility with an abdominal mass of 2 months duration that progressively increased in size. She denied any vaginal bleeding or abdominal pain. The patient noticed a decline in appetite and body weight by 6 kg within the last 2 months. The patient had her menarche at 14 years and experienced regular menstrual cycles until menopause at age 49 years. She is nulliparous and has a history of primary infertility, never having achieved pregnancy despite being sexually active without contraception for many years. The patient had used oral contraceptives in the past but had discontinued their use several years prior to menopause. The patient had neither urination nor defecation disturbances. She had no personal or family history of endometriosis and malignancy. Physical examination revealed a mobile abdominal cystic mass measuring 30×30×10 cm accompanied by ascites. Other external and internal genitalia examinations were all within normal limits. No abnormality was found in any haematological or biochemical panels. This case report is exempt from ethics review as the case does not involve any restricted health services to the patient. The patient was fully informed about the nature of the report and has provided her consent to participate.

INVESTIGATIONS

Transabdominal and transvaginal ultrasonography results showed a hypoechoic mass measuring >14.60×12.55 x13.51×11.49 cm, with septa and papillary projections, and a colour score of +2. Ascites was also detected. The uterus and contralateral adnexa were difficult to identify due to the large mass. In conclusion, based on the IOTA Simple Rules, this mass would be classified as malignant, because it meets the criteria for M2 (ascites) and M4 (irregular multilocular solid tumour ≥100 mm) features (figure 1). Serum markers for cancer antigens (cancer antigen 125, cancer antigen 19-9) were within normal limits. No additional imaging was performed due to limited coverage from the National Health Insurance.

TREATMENT

Due to suspicion of ovarian cancer, a laparotomy was performed. During the operation, approximately 1600 cc of yellowish ascitic fluid was found.

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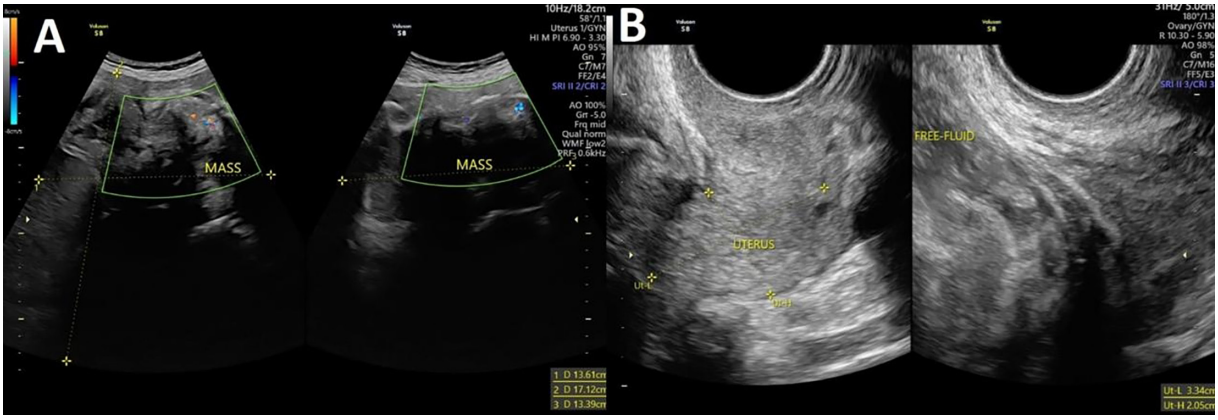

Figure 1 (A) Transabdominal ultrasound showing right ovarian cystic mass. (B) Transvaginal ultrasound showing right ovarian cystic mass.

On further exploration, a yellowish cystic mass measuring 21×22×10 cm with an irregular surface was spotted. This mass originated from the right ovary and was adhered to the uterus, rectum, sigmoid colon, and lateral and posterior peritoneal wall (figure 2). Furthermore, an irregular surface mass measuring 8×7×5 cm was found, which originated from the left ovary. Consequently, we performed a total hysterectomy and bilateral salpingo-oophorectomy, then sent for a frozen section examination (figure 3). The frozen section result revealed an endometrioma of the right ovary. Histopathological examination confirmed the diagnosis of bilateral ovarian endometrioma, and there was no evidence of malignancy in the uterus. While cytology of the ascitic fluid should have been ideal in malignant cases, since we performed a frozen section to the ovarian tumour and showed a benign lesion of endometrioma, therefore we did not continue to perform surgical staging that was only useful for malignant cases.

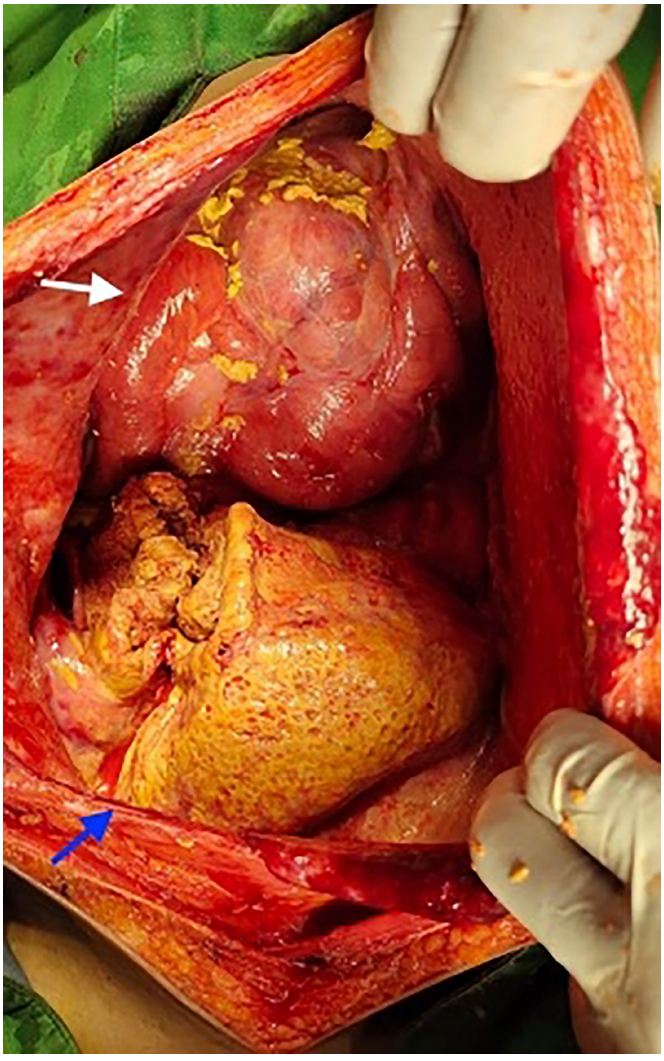

Figure 2 Intraoperative photograph showing ruptured cystic mass (blue arrow) with ileum–jejunum–omentum joined together (white arrow).

OUTCOME AND FOLLOW-UP

Around 2 weeks after the surgery, the patient visited the outpatient clinic without any complaints, and the surgical wound had completely healed. We explained that the pathology results showed a benign lesion of the ovary, which still carried a risk of recurrences and malignant transformation. The risk of malignant transformation might originate from microscopic lesions from the ruptured mass during surgery. Therefore, we suggested that the patient undergo routine gynaecological examinations every 3 months for at least 5 years.

DISCUSSION

Endometriosis is a chronic inflammatory disease characterised by the functioning of endometrial glands and stroma outside the uterine cavity.[1] Endometriosis in postmenopausal women is

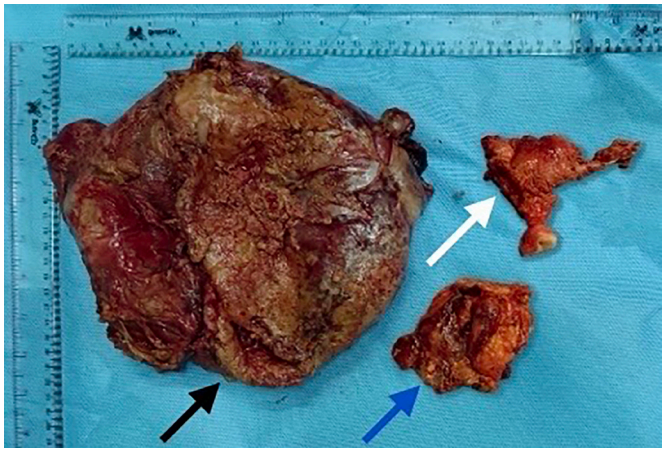

Figure 3 Specimens after surgery showing right adnexa (black arrow), uterus (white arrow) and left adnexa (blue arrow).

rare, with an estimated incidence of 2–5%.[4] It typically occurs in individuals who have undergone hormone replacement therapy (HRT) and is rarely found in those without a history of HRT or tamoxifen treatment.[7] Postmenopausal endometriosis is mostly found in the ovaries, accounting for approximately 79% of cases, as in our case.[4]

The exact pathogenesis of endometriosis is still unknown. However, regardless of its origins, endometriosis is widely recognised as a disease that depends on oestrogen. There are three classic theories for endometriosis aetiology: (1) Sampson's theory, (2) Meyer's theory and (3) Halban's theory. The most renowned theory is Sampson's pathophysiology theory of retrograde bleeding. However, the fact that endometriosis lesions can develop and persist in postmenopausal women, who do not have menstrual cycles or high levels of oestrogen, contradicts this theory and suggests that there may be another mechanism at play.[8] On the other hand, Meyer's theory postulates that endometriosis originates from metaplasia of coelomic epithelium, while Halban's theory suggests that endometriosis lesions stem from haematogenous or lymphogenous spread of viable endometrial cells.[9]

Excess oestrogen is one of the main factors that promote endometriosis. The mechanism of postmenopausal endometriosis is even more complex. Postmenopausal endometriosis can occur as either a recurrence or continuation of premenopausal disease or as a de novo condition. De novo endometriosis, as in our case, often develops in obese patients or those receiving HRT.[4 10 11] Oestrogen stimulates endometrial proliferation and ectopic lesions can enhance oestrogen sensitivity, thereby increasing the risk of developing endometriosis.

In contrast, progesterone may suppress this promoting action of oestrogen.[10] Therefore, endometriosis in postmenopausal women who are receiving HRT should always be considered, especially those who received unopposed oestrogen therapy. Clinicians prescribing HRT to postmenopausal women should be aware of this condition. Our patient is a postmenopausal woman in her 60s who has never received any form of HRT and is obese. Following the cessation of oestrogen production at the ovaries, peripheral oestrogen production from androgen conversion (particularly in adipose tissue and skin) takes over. Obese postmenopausal women have more adipose tissue, which leads to higher levels of endogenous oestrogen and an increased risk of endometriosis.[4] Another rationale for our case is that she may have had undiagnosed endometriosis during her premenopausal years. Without comprehensive gynaecological sonography records, it is difficult to rule out this hypothesis.

Typical symptoms of postmenopausal endometrioma are non-specific, ranging from pelvic pain, adnexal cystic mass or intestinal symptoms. When presented with a case of an adnexal mass in postmenopausal women, one must always evaluate the possibility of a malignant ovarian tumour. Postmenopausal endometriosis warrants more attention in cases with risk factors such as HRT, obesity or a previous history of endometriosis. Differentiating benign and malignant tumours in the postmenopausal population can be difficult.[4 12] Postmenopausal endometriosis, for one, may have similar presentations to malignant disease as it can also infiltrate adjacent tissues and organs.[13] In addition, ovarian endometrioma has similar risk factors to ovarian cancer, that is, longer lifetime oestrogen exposure (low parity, infertility, late childbearing age, early menarche, late menopause and oral contraceptive use).[5 6] Our patient is a P0A0 postmenopausal woman who had her menopause in her late 40's with a history of oral contraceptive use, implying longer oestrogen exposure. We initially suspected ovarian cancer in this case considering her age, risk factors and presentations that are highly suggestive of an ovarian malignant tumour.

We also found M2 and M4 features (presence of ascites and an irregular multilocular solid tumour with the largest diameter >100 mm) on both her transabdominal and transvaginal ultrasonography (TVS). The IOTA group developed a classification system for adnexal lesions comprising four Easy Descriptors for benign lesions and two for malignant ones. Alternative methods, such as the Simple Rules, can be employed for lesions that cannot be categorised using Easy Descriptors. These Simple Rules rely on five ultrasound characteristics indicating benign lesions (B-features) and another five features suggesting malignancy (M-features). Lesion classification is based on the exclusive presence of either B-features or M-features. If both types of features appear simultaneously or no features are detected, the lesion is deemed unclassifiable. The popularity of the IOTA Simple Rules has grown due to their ease of use, which does not require computer calculations. Recognition of this method is evident from its adoption by various professional organisations. The Royal College of Obstetricians and Gynaecologists (RCOG) incorporated the Simple Rules into their Green-top Guideline in 2011 for managing adnexal masses in premenopausal women. The American College of Obstetricians and Gynecologists followed suit in 2016 by integrating the Simple Rules into their clinical guidelines. Notably, in 2017, a first international consensus report acknowledged the Simple Rules as the primary diagnostic strategy for evaluating adnexal masses.[14]

The TVS has been considered the first-line examination for pelvic endometriosis due to its highly accessible, inexpensive and well-accepted nature. Endometriomas, as in our case, have specific characteristics on USG, namely unilocular cysts with a ground glass appearance. However, TVS is operator dependent and only offers a very restricted field of view. MRI has offered a solution to these limitations and has become very useful in helping diagnose ovarian endometriotic cysts and deep infiltrating endometriosis. Moreover, MRI might also be useful when expanded pelvic adhesion is suspected. CT scans help in diagnosing patients with suspected bowel endometriosis or those with genitourinary involvement.[4 13 15]

There is no specific serum biomarker for endometriosis. Several biomarkers, including CA-125, cytokines, angiogenic and growth factors, are known to increase in women with endometriosis. However, these biomarkers are non-specific and can also be found in other pathologies, including malignancies.[1]

Surgery is the mainstay first-line treatment for endometriosis, particularly in cases of new-onset endometriosis. According to the RCOG Green-top Guideline No 62, adnexal masses of 5 cm or more require evaluation and excision if they do not resolve spontaneously in postmenopausal women.[16] The European Society of Human Reproduction and Embryology guideline on endometriosis states that laparoscopy is the gold standard for diagnosing endometriosis, even in postmenopausal women.[17]

Surgery followed by histological examination is currently the gold standard for diagnosing endometriosis, regardless of age and menopausal status. This approach allows for simultaneous diagnosis and treatment of endometriotic lesions. However, recurrences are common following surgical therapy; therefore, second-line drugs (such as progestogens, aromatase inhibitors, etc) should be considered.[8] Postmenopausal endometriosis carries a risk of malignant transformation. According to Kobayashi *et al*, approximately 0.72% of patients with ovarian endometriomas develop ovarian cancer, with a higher risk in postmenopausal women.[18] This risk increases with age, with studies showing that up to 2–3% of ovarian endometriomas in postmenopausal

women may undergo malignant transformation.[19] Therefore, comprehensive follow-up after surgery is recommended in such cases.

Patient's perspective

I was relieved by the result of the tumour showed a benign tumour. However, I understand that the tumour may have the possibility to convert into cancer and therefore I should maintain my physical health well. I will also come for a routine gynaecology check-up to make sure the tumour has not grown back.

Learning points

- Postmenopausal endometriosis is rare and may present with signs and symptoms suggestive of malignancy.
- Approximately 2–3% of patients with ovarian endometrioma are at risk of developing malignant transformation into ovarian cancer, particularly clear cell carcinoma and endometrioid type carcinoma.
- Comprehensive surgical management and follow-up after surgery are recommended in such cases. The risk of malignant transformation might originate from microscopic lesions from the ruptured mass during surgery.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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