CASE REPORT

Detection and differential diagnosis of suspected malignant transformation of an endometrioma during pregnancy

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SUMMARY

Asymptomatic female in her early 30s presented for her singleton nuchal translucency ultrasound at 12.4 weeks of gestational age. No fetal abnormalities were seen. A large maternal left adnexal mass was identified, prompting a transvaginal ultrasound. The findings were felt to be consistent with an endometrioma, albeit with a 1 cm solid nodule. At this point, the diagnosis was considered to likely represent a decidualised endometrioma; however, warranting careful follow-up. The 20-week anatomy scan demonstrated an enlarging solid nodule that now contained vascularity within the left adnexal mass prompting an MRI. These features were more suggestive of malignancy, although a decidualised endometrioma, which can demonstrate intrapartum growth and vascularity, remained in the differential. Intrapartum sonographic surveillance documented progressive growth. The lesion was uneventfully removed at the time of delivery. Pathology showed clear cell carcinoma within an endometrioma.

BACKGROUND

The most practical modality to assess an adnexal mass is transvaginal ultrasonography owing to its availability and high negative predictive value. Masses can accurately be classified as low risk or high risk based on sonographic morphological analysis.¹ Colour Doppler ultrasound and spectral Doppler waveform characteristics often help with further characterisation of these lesions.¹ However, MRI plays a key role in problem solving when sonographic findings are indeterminate. Although MRI is increasingly accurate in diagnosis, it is better reserved for these indeterminate cases owing to its comparatively decreased availability and increased cost. As MRI contrast agents are not administered intrapartum, the evaluation of intraleisional vascularity is limited.

Endometriosis is a gynaecological disorder that primarily affects women during their reproductive years, occurring as a result of functional endometrium located outside of the uterus. The spectrum of disease ranges from microscopic endometriotic implants to large cysts known as endometriomas. Endometriosis most commonly affects the ovaries.

Cases of malignant tumours arising in patients with endometriosis were first reported in 1925 by Sampson.² Since that time, malignant transformation has become a well-documented, albeit rare (<1% of cases), complication of endometriosis.³ The haemorrhagic process of endometriosis

predisposes to endometrial malignancies.⁴ The most common malignant neoplasm arising from endometriosis is endometrioid carcinoma, followed by clear cell carcinoma.^{5 6}

Women affected by ovarian cancer related to endometriosis are usually 10–20 years younger than those affected by ovarian cancer without endometriosis.⁷ Early detection of malignancy is the key to improving prognosis and preserving fertility of these younger patients.⁷

Our case demonstrates the use of imaging to detect malignant transformation of an endometrioma and discusses the differential diagnosis and potential mimickers of malignancy on imaging evaluation.

CASE PRESENTATION

Asymptomatic female in her early 30s presented for her singleton nuchal translucency ultrasound at 12.4 weeks of gestational age (figures 1–4). She had no history of endometriosis or other significant medical or surgical history.

INVESTIGATIONS

No fetal abnormalities were seen on the nuchal translucency ultrasound. A large maternal left adnexal mass was identified, prompting a transvaginal ultrasound. The findings were felt to be consistent with an endometrioma, albeit with an avascular 1 cm solid nodule.

Figure 1 Transvaginal ultrasound performed at 12.4 weeks gestation demonstrated a complex left adnexal mass measuring 7.7×6.8×5.0 cm. It contained homogeneous low-level internal echoes and a 1 cm echogenic avascular mural nodule (dashed arrow). A separate left ovary was not identified.

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Figure 2 Twenty-week ultrasound showed that the overall size of the mass was unchanged while the solid nodule had increased in size from 1 cm to 3.8×3.3×2.7 cm and now demonstrated vascularity.

Evaluation at the time of the 20-week anatomy ultrasound demonstrated an enlarging solid nodule that now contained vascularity within the left adnexal mass prompting an MRI evaluation.

The MRI was equivocal as to whether this represented a decidualised endometrioma or malignant degeneration within an endometrioma. MRI was limited by the inability to assess vascularity as Gadolinium, a class C drug, is contraindicated intrapartum.

Subsequent intrapartum sonographic surveillance documented the mass and solid nodule continuing to grow reaching maximal dimensions of 10 and 5.6 cm, respectively.

DIFFERENTIAL DIAGNOSIS

Malignant degeneration of an endometrioma is generally due to either endometrioid or clear cell carcinoma. Endometrioid carcinoma is the second most common epithelial malignancy representing 20%–25% of ovarian malignancies. Approximately 15%–20% are associated with endometriosis, which may occur within the endometriosis, the ipsilateral or contralateral ovary.⁸

Clear cell carcinoma is considered to be of müllerian duct origin and a variant of endometrioid carcinoma. It constitutes 5–10% of ovarian malignancies. Associated pelvic endometriosis is present in 50–70% of clear cell carcinomas and approximately 33% arise within the lining of the endometrioma.⁸

Another neoplasm considered in the differential diagnosis was a cystadenoma of low malignant potential (LMP). LMP tumours have cytological features of malignancy, but do not invade the stroma, and thus have a much better prognosis. One of the sonographic appearances described for LMP tumours is a cyst containing uniform low-level echoes (similar to an endometrioma) with vascular mural nodule(s).⁹ Ovarian dysgerminoma also occurs not uncommonly in pregnancy, but this entity was not considered as these tumours are usually solid in nature.

The variable sonographic features of endometriomas may overlap with a variety of benign and malignant ovarian masses. Classic characteristics of endometriomas include diffuse low-level internal echoes and echogenic wall foci. Septations, thickened walls and wall nodularity may also be seen in endometriomas.³

In the context of both the multiplicity and MRI signal intensity of lesions, according to Togashi *et al*, when a cyst was hyperintense on T1-weighted images and demonstrated shading on T2-weighted images, a ‘definitive’ diagnosis of an endometrioma was made.¹⁰ When T1-weighted images showed multiple

Figures 3 (A–C) The below three images are from MRI pelvis without gadolinium at week 22 of pregnancy, which demonstrated a 7.7×4.1×4.9 cm complex adnexal mass arising from the left ovary. The cystic component of the mass demonstrated bright signal on T1-weighted image (T1WI) and T2WI, suggestive of blood and blood products. The solid component of the mass measured 4.1×3.3 cm, unchanged from previous ultrasound, and had a homogeneously intermediate signal on T1WI and mildly bright signal on T2WI. No evidence of ascites or pelvic lymphadenopathy. The differential diagnosis included a decidualising endometrioma of the ovary or a neoplastic ovarian process such as an endometrioid carcinoma within an endometrioma. (A) Axial FSPGR T1 of the pelvis demonstrated the homogeneously intermediate signal of the solid component of the mass (arrow) and the bright signal of the cystic component (dashed arrow). (B) Axial FrFSE T2 demonstrated the mildly bright signal of the solid component of the mass (arrow) and the bright signal of the cystic component (dashed arrow). (C) Coronal FIESTA T2 demonstrated a rind of ovarian tissue (arrow) surrounding the complex lesion, confirming its origin from the ovary. FIESTA, fast imaging employing steady-state acquisition; FrFSE, fast-recovery fast spin-echo; FSPGR, fast spoiled gradient-recalled-echo.

hyperintense cysts, regardless of their T2-weighted signal intensity, a ‘definitive’ diagnosis was also made.¹⁰

There are also key imaging findings that suggest malignant transformation of an endometrioma. While endometriomas contain haemorrhage and may have irregular and thickened

Figure 4 Final ultrasound at 32 weeks showed a further increase in overall size of the left adnexal mass, which now measured 10×6.7×6.5 cm. The solid component had also increased in size, now measuring 5.6×4.7×5.2 cm (compared to 4.5×4.4×4 cm at 28-week ultrasound). Considering the rapid increase in size of the solid vascular component, malignancy was the most likely diagnosis, although decidualisation remained a possibility.

walls, they do not typically demonstrate enhancing solid projections.¹¹ The most important finding which suggests malignant change is the presence of a vascular nodule on ultrasound or a contrast-enhancing nodule on MRI.⁷ On T2-weighted images, when the mass loses its characteristic shading, either due to tumour secretions diluting the thick haemorrhagic fluid or because of increase in size of the endometrioma, malignant transformation may be suggested.¹² However, this finding may also be seen in benign endometriomas. Small enhancing nodules on T1-weighted images postcontrast within a hyperintense endometrioma may be detected with the help of dynamic subtraction MRI.⁷

There are several instances to be aware of in order to avoid mistakenly diagnosing malignant transformation within an endometrioma. First, the surrounding ovarian parenchyma may resemble the enhancing solid malignant component of an endometrioma. The key findings to confirm this represents compressed ovarian tissue are the presence of follicles and the 'crescent' sign.⁷

Second, malignant mural nodules may be mimicked by intracystic blood clots that can demonstrate different levels of signal intensity. On ultrasound, characteristic findings for a blood clot include the presence of fine interdigitating reticulations, retractile margins and evolution over time. On MRI, the tissue characteristics and lack of enhancement would indicate a blood clot.⁷

Rarely, in a pregnant patient, a solid vascular mural nodule may be seen within an endometrioma owing to decidual changes of the ectopic endometrium that may mimic malignant change. On fast spin-echo T2 MRI, the mural nodules in decidualisation are similar to normal endometrium or placenta. On spin-echo T1-weighted images (T1WI), they are similar to normal myometrium with low signal intensity. The different morphological appearances of these nodules can include linear, small nodular, broad-based nodular or polypoid. Preliminary work suggests that the apparent diffusion coefficient of decidualised mural nodules is higher than in malignant nodules. If these findings are observed, close follow-up is required to rule out malignancy.¹³

As Woodward *et al*³ describe, the presence of solid components, thick or irregular septations, and a size that is larger than expected for an endometrioma, are all features to suggest malignancy. In this context, our case was suspicious for malignancy

on the basis of a vascular solid rapidly growing nodule. Decidualisation, a mimicker of malignancy, could not be excluded from the differential initially. Subsequent rapid growth of both the lesion and the vascular nodule were indicators of malignancy.

TREATMENT

The lesion was considered most likely to represent malignant degeneration in an endometrioma. The patient was counselled about the risks of malignancy, but chose not to undergo an intrapartum procedure owing to the potential risk of preterm labour. The left adnexal mass continued to grow reaching a maximum dimension of 10 cm with the solid nodule growing to a maximum dimension of 5.6 cm. The adnexal mass was uneventfully removed at the time of delivery.

OUTCOME AND FOLLOW-UP

The pathological diagnosis was clear cell carcinoma within an endometrioma.

4 months later, a staging procedure was performed via elective robotic-assisted hysterectomy, right salpingo-oophorectomy, pelvic and periaortic lymph node dissection and omentectomy. Pathology identified no evidence of malignancy. It was elected to administer adjuvant carboplatin/Taxol chemotherapy on the basis that it is generally well tolerated and the patient is of young age.

DISCUSSION

The management of potential malignancy in pregnancy is generally multifactorial. A multidisciplinary team approach should be used when imaging cannot confidently establish a benign diagnosis. The aim is to properly select patients requiring surgical intervention and to optimise the timing of this intervention. In an asymptomatic patient, surgery should be considered for ovarian lesions that persist or increase in size on surveillance imaging, do not demonstrate characteristic benign sonographic features or show suspicious findings including irregular thick septations, papillary excrescences, vascular mural nodules or interval growth.¹⁴ Laparoscopic surgery during the first or second trimester is not associated with significant increased incidence of preterm labour, fetal loss or teratogenicity. Laparoscopic surgery during the third trimester is associated with preterm labour.

There are at least 22 cases reported in the literature of decidualised ovarian endometriosis in pregnancy in which sonographic and colour Doppler examination documented rapidly growing and vascularised intralesional excrescences, similar to the appearance of malignancy within an ovarian endometrioma.¹⁵ Thus, an initial expectant management with serial follow-up is appropriate in the absence of other features of malignancy such as thick irregular septations or ascites. Ca-125 levels are not useful as they are physiologically elevated in pregnancy.

The patient in our case was referred for multidisciplinary consultation after the follow-up studies which demonstrated interval growth, and ultrasound and MRI could not definitely distinguish a benign lesion from a malignant lesion. The patient was counselled about the risks of malignancy, but chose not to undergo an intrapartum procedure owing to the potential risk of preterm labour. Removal of the left ovarian mass was scheduled to be performed at the time of an elective caesarean section.

Finally, our case highlights the importance of ultrasound in pregnant patients with adnexal masses. There are inherent

limitations to the use of MRI in pregnancy. According to ACR guidelines, there is no known adverse effect of MRI on the fetus and the decision to scan during pregnancy should be made on an individual basis.¹⁶ In pregnancy, intravenously administered gadolinium agents cross the placenta and enter the fetal circulation, subsequently being excreted into the amniotic fluid.¹⁶ These agents should be avoided in pregnancy as their effects on the fetus are not well understood.¹⁶ Nevertheless, usage should be guided by a risk–benefit ratio in combination with informed consent and documentation.¹⁶ In our experience, MRI failed to provide more definitive information than ultrasound. In fact, ultrasound provided the information of internal vascularity, which in the absence of gadolinium administration could not be readily defined on MRI. Furthermore, ultrasound could readily and effectively be used to follow our patient multiple times during her pregnancy.

Learning points

- ▶ It is important to be aware of malignant degeneration of an endometrioma.
- ▶ This case highlights the importance of high-quality ultrasound and the limitations of unenhanced MRI in pregnant patients.
- ▶ The most important finding which suggests malignant change of an endometrioma is the presence of a rapidly growing vascular nodule on ultrasound.
- ▶ Common mimickers of malignant transformation within an endometrioma are
 - The surrounding ovarian parenchyma that may resemble the enhancing solid malignant component of an endometrioma.
 - Intracystic blood clots that can demonstrate different levels of signal intensity, appearing like malignant mural nodules.
 - A solid vascular mural nodule resembling malignancy that may be seen within an endometrioma owing to decidual changes of the ectopic endometrium in a pregnant patient.

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