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Grade 3 endometrioid adenocarinoma of the lower uterine segment diagnosed 6 weeks after a term delivery: A case report and literature review

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ABSTRACT

Background: Endometrial cancer is the most common gynaecological malignancy in Australian women. Less than 5% of cases occur in women under 40 years of age and it is rarely associated with pregnancy. Most cases associated with pregnancy are diagnosed after first trimester loss. Only 14 cases of endometrial cancer diagnosed post-partum are reported in the literature. These cases were diagnosed up to 15 months post-partum. The histopathological classification was low grade in 12 patients and high grade in two patients.

Case: We describe a 37 year old woman, who presented after her second vaginal delivery (at 37 weeks of gestation) with suspected retained products of conception (RPOC). She had a dilation and curettage leading to the diagnosis of endometrial cancer six weeks post-partum. She underwent a total laparoscopic hysterectomy, bilateral salpingo-oophorectomy and bilateral sentinel node biopsy. Histopathology confirmed a stage 1B grade 3 endometrioid adenocarcinoma located in the lower uterine segment with widespread lymph-vascular invasion and no other evidence of malignancy. She is planned to complete six cycles of adjuvant carboplatin/ paclitaxel chemotherapy, followed by pelvic external beam radiotherapy.

Discussion: We report the second case of a high-grade endometrial cancer diagnosed post-partum. The bulk of this tumour was in the lower segment of the uterus, which together with the fundal placenta, likely permitted the pregnancy progressing to term. Endometrial cancer should be considered a rare cause of abnormal post-partum bleeding. Curettage and histopathology examination is recommended in cases that do not resolve with conservative measures to exclude this rare complication.

1. Introduction

Endometrial cancer is the most common gynaecological cancer and the fifth most prevalent cancer in Australian women (Australian Institute of Health and Welfare Cancer, 2019). It is usually seen in peri- and post-menopausal women, with a median age of 61 years at diagnosis and less than 5% of cases reported in women less than 40 years of age (Soliman et al., 2005). The co-existence of endometrial cancer and pregnancy is rare. Of cases reported in the literature, the majority were incidentally diagnosed in early pregnancy, after dilation and curettage for spontaneous miscarriage or elective abortion (Yael et al., 2009; Shiomi et al., 2019). To the best of our knowledge there have only been 14 cases of endometrial cancer diagnosed post-partum reported in the last 40 years. Here, we report a rare case of grade 3 endometrioid adenocarcinoma of the uterus diagnosed six weeks after a term normal vaginal birth and review the relevant literature.

2. Case report

A 37-year-old Caucasian woman, gravida 2 para 1, presented at 34 weeks of gestation in an uncomplicated pregnancy with an unprovoked, painless, antepartum hemorrhage of approximately 15 mL. Her history included a normal vaginal birth at 41 + 6 weeks of gestation three years earlier. She had no significant gynaecological, medical or surgical history and a normal body mass index of 20 kg/m^2. Her family history included breast cancer in her paternal grandmother and aunt.

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Ultrasound showed fundo-posterior placenta which was not low lying and normal fetal growth and wellbeing. Quantitative test for feto-maternal haemorrhage was negative. The bleeding resolved spontaneously and she was discharged home. At 37 weeks of gestation she had a normal vaginal birth of a baby weighing 3345 g. Her estimated blood loss at delivery was 350 mL. The placenta was complete but the membranes were incomplete. Hence she was treated with a 40 unit oxytocin intravenous infusion and prophylactic ampicillin, metronidazole and gentamicin. She remained clinically well and was discharged home the following day with a five day course of oral amoxicillin and clavulanic acid.

She re-presented to hospital six days post-partum after passing a small amount tissue vaginally. Histopathology confirmed retained products of conception (RPOC) (Fig. 1A). Pelvic ultrasound demonstrated 12 mL of suspected RPOC and an endometrial thickness of 26 mm. She was expectantly managed at this time and continued oral antibiotics for a further three days. A repeat pelvic ultrasound on Day 29 post-partum showed an endometrial thickness of 37 mm and that the material within the endometrial cavity had increased in volume to 30–40 mL and was more vascular (Fig. 2). A dilation and curettage for suspected RPOC was arranged and undertaken on day 37. Histopathology showed Grade 3 endometrioid adenocarcinoma with no evidence of RPOC (Fig. 1B). A computed tomography scan of her chest, abdomen and pelvis showed a bulky uterus and no metastatic disease.

The patient was immediately referred to our tertiary Gynaecological Oncology centre. After a multidisciplinary review of the pathology and imaging, a total laparoscopic hysterectomy, bilateral salpingo-oophorectomy and bilateral sentinel node biopsy was performed. Histopathology confirmed the diagnosis of Stage IB Grade 3 endometrioid adenocarcinoma, lying in the lower segment of the uterus, invading into the outer half of the myometrium with no involvement of the cervical stroma (Figs. 1C and 3). There was widespread lymph-vascular invasion, including in the left parametrium with no direct invasion present. Immunohistochemistry was positive for oestrogen receptors, weakly positive for progesterone receptors with loss of staining on MLH1 and PMS2 protein. MLH1 promoter methylation was inconclusive and serum genetic testing for Lynch Syndrome did not identify any mutations. All sentinel nodes (0/4) showed no evidence of malignancy and peritoneal cytology was normal. The patient completed six cycles of adjuvant paclitaxel and carboplatin chemotherapy, followed by 45 Gray of pelvic external beam radiotherapy. The patient remains well, with no evidence of disease recurrence at 12 month follow up.

3. Discussion

Endometrial cancer is usually an oestrogen-dependent neoplasia that usually occurs in post-menopausal women. Due to the younger age and high progesterone levels it is considered to be unusual during pregnancy. The co-existence of endometrial cancer and pregnancy may reflect either pre-existing endometrial neoplasia or onset during pregnancy (Yael et al., 2009). Young patients with pre-existing endometrial neoplasia are likely to have difficulty conceiving, due to the cancer creating a hostile endometrium that precludes implantation and embryo growth. In cases where implantation does occur the developing cancer most often leads to early miscarriage as evidenced by previous reports (Yael et al., 2009; Shiomi et al., 2019). Conversely, pregnancy should not promote the development and growth of endometrial cancer due to augmented progesterone secretion and a decreased oestrogenic state.

To investigate this rare condition we performed a literature review of endometrial cancer diagnosed post-partum. We completed a search of PubMed and MEDLINE databases for English articles in the period between January 1980 to January 2021, using the following keywords “endometrial cancer”, “endometrial carcinoma”, “endometrioid cancer”, “endometrioid carcinoma”, “pregnancy” and “postpartum” in various combinations. Thirteen studies with 14 cases of endometrial cancer in the postpartum period were reviewed and are summarised

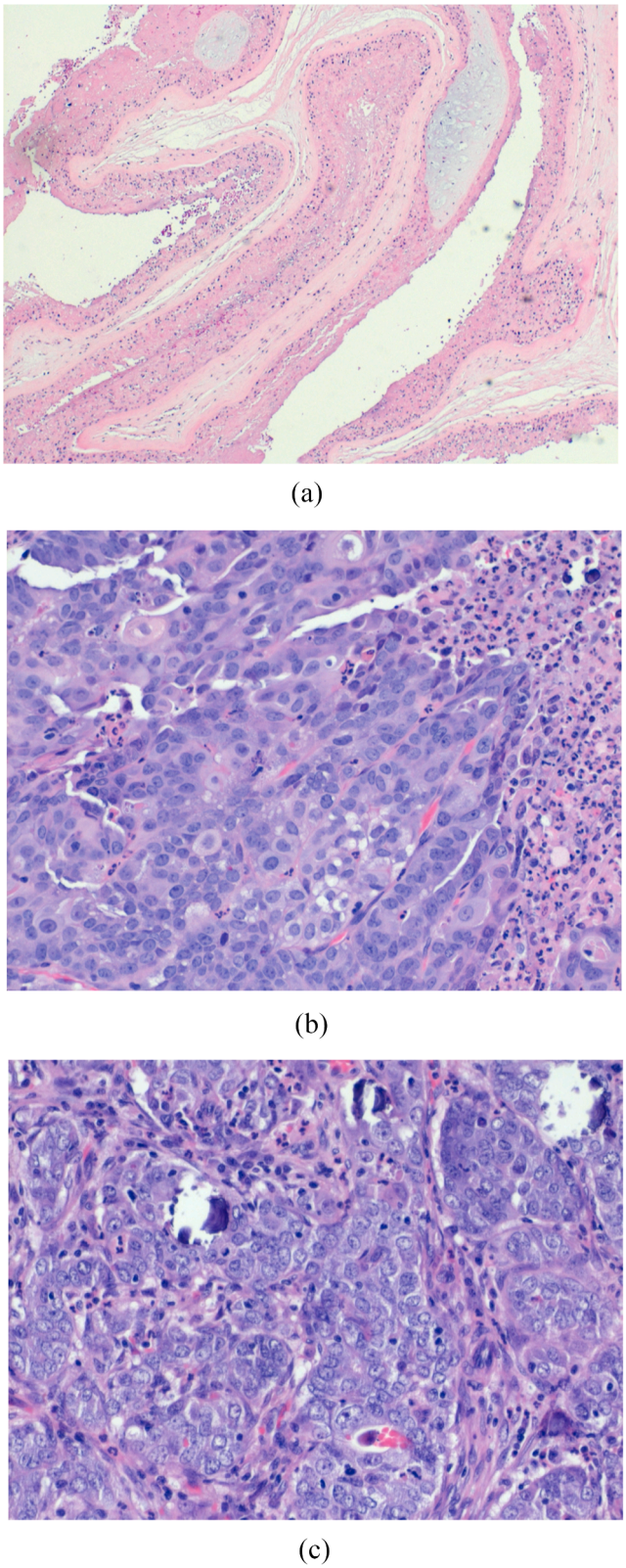

Fig. 1. Histopathology demonstrating A) retained products of conception; B) curette sample showing high grade endometrioid adenocarcinoma; C) surgical specimen showing grade 3 endometrioid adenocarcinoma.

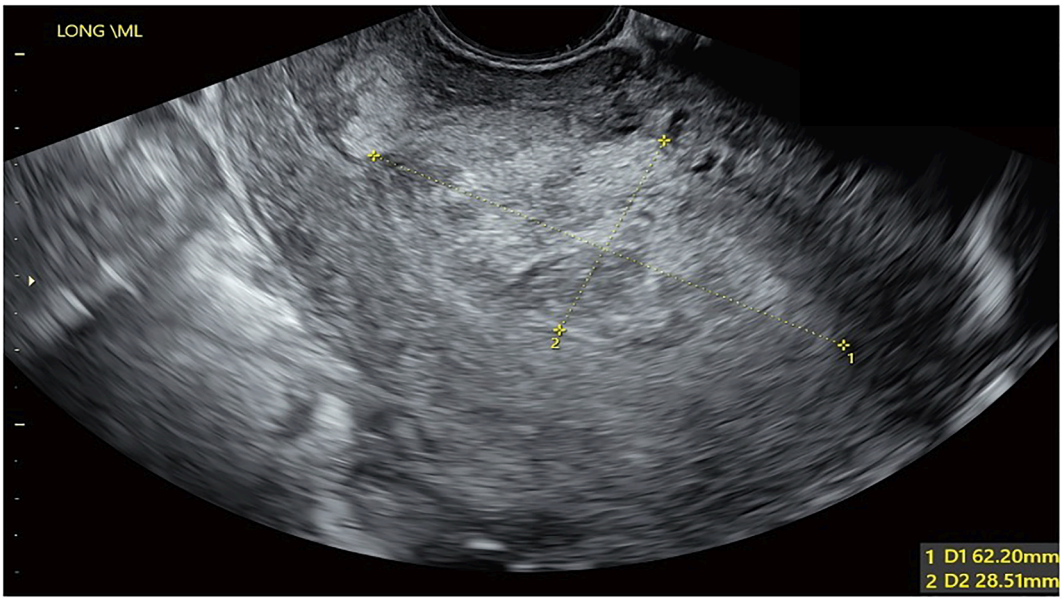

Fig. 2. Ultrasound image showing heterogenous material measuring 62 × 29 × 44 mm (40 mL) within the endometrial cavity, endometrial thickness 37 mm and normal myometrium.

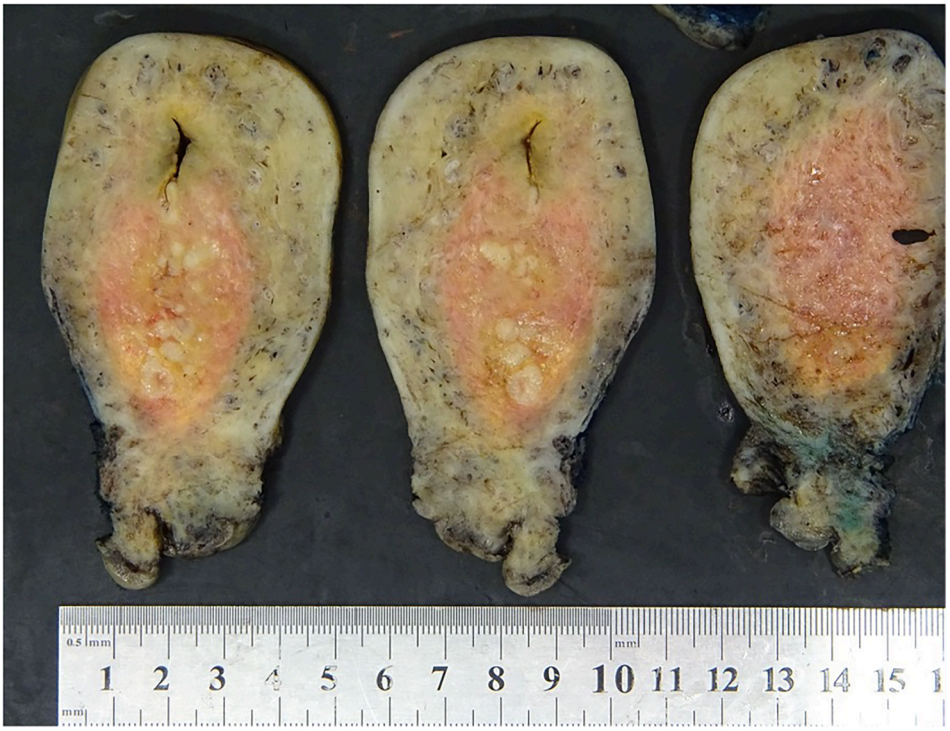

Fig. 3. Operative macro-specimen.

below and in Table 1.

Risk factors

Risk factors for endometrial cancer include age, prolonged unopposed oestrogen exposure, as seen in obesity and polycystic ovarian syndrome, and genetic syndromes including Lynch Syndrome. Our literature review found that two patients were reported to have a history of anovulation and one patient had endometrioid carcinoma that was conservatively managed prior to pregnancy.

The majority of patients with pregnancy associated endometrial cancer did not have any risk factors identified.

Chronological age and gestational age

Amongst women described in the literature as developing endometrial cancer during pregnancy the median age at diagnosis was 32 years (range from 22 to 40 years). Eight cases presented after term deliveries and five after pre-term delivery (28 to 35 weeks).

Presenting complaint

The most common presenting complaint identified was abnormal vaginal bleeding in the postpartum period. Two cases were diagnosed from histopathology taken during caesarean section. The first where an endometrial curettage was performed at the time of caesarean section at 28 weeks of gestation for preterm prelabour

Table 1
Summary of 14 pregnancy associated endometrial cancer cases.

Age (median, years)	32
Parity (n, %)	
Nulliparous	2 (14.3)
Multiparous	12 (85.7)
Risk factors (n, %)	
Anovulation	2 (14.3)
History of endometrial cancer	1 (7.1)
Nil	11 (78.6)
Gestation at delivery (n, %)	
Preterm	5 (35.7)
Term	8 (57.1)
N/A	1 (7.1)
Mode of delivery (n, %)	
Vaginal birth	9 (64.3)
Caesarean section	4 (28.6)
N/A	1 (7.1)
Presentation (n, %)	
PPROM	1 (7.1)
Antepartum haemorrhage	1 (7.1)
Pelvic pain	1 (7.1)
Abnormal post-partum vaginal bleeding	6 (42.9)
Ascites/oedema	1 (7.1)
Surveillance (due to history)	1 (7.1)
Time of diagnosis (n, %)	
Intra-operatively (during caesarean)	2 (14.3)
Post-partum	12 (85.7)
Time of post-partum diagnosis (median, months)	6
Histopathology (n, %)	
Endometrial adenocarcinoma	13 (92.9)
Adenosquamous	1 (7.1)
Stage	
1A	9 (64.3)
1B	1 (7.1)
1C	2 (14.3)
3C	1 (7.1)
4B	1 (7.1)
Grade	
1	10 (71.4)
2	1 (7.1)
3	1 (7.1)
N/A	2 (14.3)
Treatment	
Primary surgery (hysterectomy)	9 (64.3)
Surgical (hysterectomy) + adjuvant therapy	3 (21.4)
Chemotherapy	1 (7.1)
Other	1 (7.1)
Prognosis	
No evidence of disease (for follow up available)	9 (64.3)
Death	1 (7.1)
N/A	4 (28.6)

rupture of membranes, The second where a caesarean hysterectomy was performed at 35 weeks of gestation for suspected placenta accreta. The authors did not indicate whether there was a suspicion of neoplasia intra-operatively. The remaining cases were diagnosed after delivery and the timing of postpartum diagnosis was highly variable, occurring up to 15 months post-partum.

Histopathology

The histopathological classification previously reported cases included eleven patients with low grade disease and one patient with high grade disease. Twelve of the cases were FIGO stage 1 and treated with primary surgery, with no evidence of disease recurrence over the reported follow up period (1 to 6 years). One patient had stage 3 disease with a survival of 8 months, and one patient had stage 4 disease, however the survival was not reported.

This case is the second report of a high-grade endometrial cancer presenting post-partum after a normal vaginal delivery. The deeply invasive endometrial cancer complicating this pregnancy may explain the antepartum haemorrhage. The RPOC passed in the post-partum period did not reveal the tumour and the deeply invasive cancer was only detected after a curettage. However, the increase in the volume of the suspected RPOC at the repeated pelvic ultrasound was thought to be unusual. The bulk of this tumour was in the lower segment of the uterus, which together with the fundal placenta, likely permitted the pregnancy progressing close to term.

Endometrial cancer located in the lower uterine segment is associated with more aggressive pathological features, including high-grade histology and lympho-vascular invasion (Jacques et al., 1997) These features were demonstrated in our case. This is distinct from the majority of cases associated with pregnancy, where the biologic behaviour is more consistent with grade I tumour commonly found in the non-pregnant population; with minimal myometrium invasion and diagnosis at earlier stage. One study reported that almost one third of women with endometrial cancer located in the lower uterine segment had underlying Lynch syndrome. This is significantly higher than the general population prevalence of 1–2% (Westin et al., 2008). Additionally, women with lower uterine segment tumours are younger at diagnosis, with a median age of 51 years (Westin et al., 2008; Hachisuga et al., 2001). In our case the lower uterine segment position of the tumour, onset of cancer at a younger age and the loss of staining for MLH1 and PMS2 prompted consideration of underlying Lynch Syndrome (Westin et al., 2008), however this was excluded after genetic testing.

In conclusion, endometrial cancer is a rare cause of abnormal post-partum bleeding. Curettage and histopathology examination should be considered in cases where vaginal bleeding does not resolve with conservative measures, especially where the volume of intracavity material increases, so that this rare complication is excluded.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2021.100884.

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