

## Case Report

# Endometrial adenocarcinoma in spontaneous abortion: two cases and review of the literature

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**Abstract:** Objectives: To report two extremely rare cases of endometrial adenocarcinoma established during the first trimester. Case presentation: A 40-year-old (gravida 0, para 0) and 33-year-old (gravida 4, para 0) woman, were diagnosed with a well-differentiated adenocarcinoma after a dilatation and curettage (D&C) for spontaneous abortions at 8 and 9 gestational weeks, respectively. Conclusions: Thirty-six cases of pregnancy-associated endometrial cancer and 20 cases of first trimester pregnancy concurrent with endometrial carcinoma have been reported as present cases in the literature. Interestingly, 15 including our two cases were detected for spontaneous abortions in first-trimester suggesting a causal correlation between endometrial adenocarcinoma and spontaneous abortions. Repeated D&C and progesterone administration may be appropriate for patients who wish to preserve fertility.

**Keywords:** Endometrial adenocarcinoma, early pregnancy, spontaneous abortions

## Introduction

Endometrial carcinomas are commonly seen in the prior post-menopausal period, and is rarely associated with pregnancy. To our knowledge, there have been thirty-six cases of endometrial cancer associated with or presumed to arise during pregnancy have been reported [1]. In most of these cases, the diagnosis was made by dilatation and curettage (D&C) for incomplete or missed abortion [1, 2]. We reports two extremely rare cases of endometrial adenocarcinoma established during the first trimester.

## Case presentation

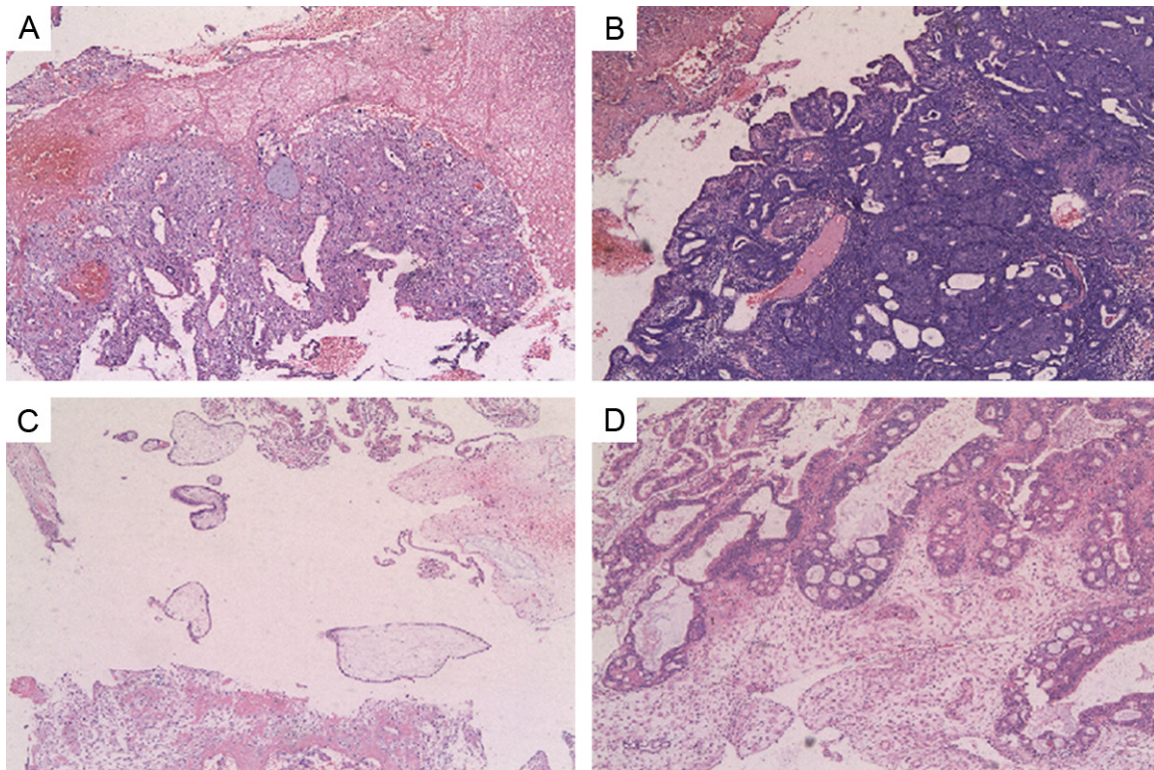
### Case 1

A 40-year-old woman (gravida 0, para 0) became pregnant and was followed up in our hospital. However, she complained of genital bleeding and abdominal pain at 8 gestational weeks. Ultrasound examination revealed no cardiac motions, and she was diagnosed with spontaneous abortion. Complete blood count, urinalysis, and coagulation studies were within normal limits. The blood human chorionic gonadotropin (hCG) level was 194.3 IU/L.

D&C was performed. There were decidua, scattering intermediate trophoblasts with a small focus of well-differentiated endometrial adenocarcinoma, with focal squamous differentiation (**Figure 1A, 1B**). Immunohistochemically, the tumor cells were positive for either estrogen receptors (ER) or progesterone receptors (PR), negative for p53. She was given oral high-dose medroxyprogesterone acetate (600 mg/d) for 20 weeks. At 16 weeks, a repeated D&C was performed, the specimen showed decidualized endometrium with no evidence of disease. The patient wished to remain fertile, so strict follow-up was planned.

### Case 2

A 33-year-old woman (gravida 4, para 0) presented with abnormal vaginal bleeding and 10 weeks of pregnancy. The ultrasonographic evaluation revealed a disordered gestational sac with a 9 weeks embryo with no heart beat. Complete blood count, urinalysis, and coagulation studies were within normal limits. The hCG level was 47458.0 IU/L, and she was diagnosed with spontaneous abortion. D&C was performed and pathology showed a well-differentiated endometrial adenocarcinoma, decidua



**Figure 1.** Concurrent endometrial adenocarcinoma and pregnancy, hematoxylin and eosin. Case 1: Decidua, scattering chorionic villi A, a focus of well-differentiated endometrial adenocarcinoma, with squamous differentiation B; Case 2: Decidua and chorionic villi, and hypersecretory endometrium with Arias Stella reaction C, well-differentiated endometrial adenocarcinoma D. Magnification: 50.

and chorionic villi, and hypersecretory endometrium with Arias Stella reaction (**Figure 1C, 1D**). Immunohistochemically, the tumor cells were positive for either ER or PR, negative for p53. The patient wished to remain fertile, so strict follow-up with repeat biopsies was planned with no therapy. Two endometrial curettage biopsy performed 2 and 4 months after the initial D&C showed no endometrial adenocarcinoma.

### Discussion

There have been 20 cases of first trimester pregnancy concurrent with endometrial carcinoma reported as present cases in the literature [1]. Interestingly, 13 of 20 cases of endometrial cancer and pregnancy in the literature were detected in first-trimester spontaneous abortions (**Table 1**). Seventeen patients, including ours had the symptom of bleeding or spotting (**Table 1**). So, the presence of endometrial cancer might have been related to the damage of chorionic villi, suggesting a causal correla-

tion between endometrial adenocarcinoma and spontaneous abortions.

In first-trimester following implantation of pregnancy, hCG promotes production of progesterone by ovarian corpus luteal cells [3, 4]. Hyperglycosylated hCG binds and antagonizes TGF $\beta$  receptors on the cytotrophoblast cells, the cells that make hyperglycosylated hCG [3]. A number of observations show that hyperglycosylated hCG can act on cancer and pregnancy implantation through antagonizing TGF $\beta$  [4]. So, when the hyperglycosylated hCG acts on cancer excessively, the hyperglycosylated hCG may also impair fetal growth and development, then lead to spontaneous abortion.

Risberg et al demonstrated endometrial carcinoma can affect the presence of estrogen sensitive but totally or partially progesterone-resistant areas in cases of nongravid secretory endometrium [5]. In these areas, there would be a condition of relative hyperestrogenism during pregnancy, which might prohibit preg-

## Endometrial adenocarcinoma in spontaneous abortion

**Table 1.** Endometrial carcinoma detected were detected in first-trimester spontaneous abortions

Authors [Reference]	Age	Symptom	Gestation/Diagnosis	Stage/Grade	Therapy	Follow-up
Schumann, et al [1]	43	Bleeding	10-12 wk, SAB	IB, G1	TAH + BSO	Ned at 20 mo
Westmann, et al [1]	40	Bleeding	Fist trim, D&C for SAB	IA, G1	TAH + BSO	Na
Karlen , et al [1]	21	Bleeding	6-8 wk, D&C for SAB	IA, G1	TAH	Ned at 6 yr
Sandstrom, et al [1]	37	Spotting	8-10 wk, EAB	IA, G1	TAH + BSO	Ned at 2.5 yr
Zirkin, et al [1]	42	Bleeding	Fist trim, D&C	IB, G1	TAH + BSO	Na
Suzuki , et al [1]	30	Bleeding	7wk, D&C for SAB	IB, G2	TAH + BSO	Ned at 5 yr
Pulitzer, et al [1]	33	Bleeding	Fist trim, SAB	IA, G1	TAH + BSO	Ned at 3 mo
Carinelli, et al [1]	40	Amenorrhea	Fist trim, EAB	IA, G1	rep D&C	Ned at 6 mo
Hoffmann, et al [1]	35	No symptoms	8-9 wk, EAB	IA, G2	TAH + BSO	Na
Orlov , et al [1]	42	Bleeding	9 wk , D&C for SAB	IA, G1	TAH + BSO	Na
Schneller, et al [1]	26	Amenorrhea	5 wk, EAB	IA, G1	rep D&C	Ned at 7mo
Kovacs , et al [1]	35	Bleeding	D&C 10 d after EAB	IB, G1-G2	BRT + TAH + BSO + RT	Ned at 1 yr
Schammel , et al [1]	38	Infertility	9 wk, D&C for EAB	IA, G1	rep D&C	Ned at 58 mo
	41	Bleeding	13 wk, D&C for SAB	IA, G1	TAH+BSO	Ned at 48 mo
	29	No symptoms	9-10 wk, EAB	IA, G1	Na	Na
	34	Bleeding	13 wk, D&C for SAB	IA, G1	PGT + D&C, TAH + BSO	Ned at 12 mo
Victoriano, et al [1]	Na	Bleeding	Fist trim, D&C for SAB	Na	Na	Na
Ayhan, et al [1]	44	Bleeding	5 wk, D&C for SAB	IA, G1	TAH + BSO + OMTX + IND	Na
Vaccarello, et al [1]	35	Bleeding	9 wk, D&C for SAB	IA, G1	TAH + BSO	Na
Hannuna, et al [1]	39	No symptoms	9 wk, D&C for SAB	IA, G1	PGT + D&C	Ned at 18 mo

Abbreviations: BSO, bilateral salpingo-oophorectomy; BRT, brachytherapy; D&C, dilatation and curettage; EAB, elective abortions; IND, lymph node dissection; mo, month; NED, no evidence of disease; Na, not available; OMTX, omentectomy; PGT, progesterone therapy; rep, repeat; RT, radiation therapy; SAB, spontaneous abortions; TAH, total abdominal hysterectomy; yr, year.

nancy implantation, fetal growth and development in first-trimester.

Immunological recognition of pregnancy was important for the maintenance of gestation, and that inadequate recognition of fetal antigens might result in failed pregnancy. CD8+ T cells and CD56+ natural killer (NK) cells, is a hallmark of the tumor immune response in first-trimester [6]. The number of CD8+ T cells increased at the border of endometrial carcinomas [7]. In contrast, only a small number of CD56+ NK cells are present in endometrial carcinomas [8]. Thus the endometrial carcinomas can alter immune response though CD8+ T cells and CD56+ NK cells, which might result in the disturbance of human endometrial immuno-microenvironment and lead to embryo rejection.

### Conclusions

Coincidental endometrial adenocarcinoma is a rare but possible event in a case of first trimester pregnancy loss. Endometrial adenocarcinoma may be the reason of spontaneous abortions, but the exact mechanism remains unknown. Most cases have the symptom of vaginal bleeding, which indirectly help to check out this rare disease earlier, the routine histological examination of the curettage specimens for all first trimester pregnancy losses should be encouraged. Nonsurgical management may be appropriate for patients who wish to preserve fertility [9].

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### Disclosure of conflict of interest

None.

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