



A case of placenta previa with increta with a history of pelvic radiation

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ABSTRACT

Background: Prior pelvic radiation increases risks of pregnancy complications that can be life threatening. No documented pregnancy has successfully occurred with pelvic radiation dosing of >45 Gy. This case report describes a successful conception after receiving 54 Gy with subsequent severe pregnancy complications.

Case

34 yo G4P2012 with a history of pelvic radiation who presented with painless vaginal bleeding at 12w6d gestation resulting from a donor egg embryo transfer. She was subsequently diagnosed with a subchorionic hemorrhage, complete placenta previa, and placenta increta leading to a gravid hysterectomy at 23w0d due to concern for hemodynamic instability.

Conclusion: History of pelvic radiation increases risk of severe life-threatening pregnancy complications. This case report details the complications that can arise to provide assistance for counseling and management for future providers.

1. Introduction

History of pelvic radiation increases the risk of pregnancy complications including abnormal placentation, fetal growth restriction, preterm labor and delivery, risk of cesarean hysterectomy, and fetal and/or maternal death. In patients with a history of undergoing high doses of pelvic radiation who are considering pregnancy or reproductive assistance, providers should consider multidisciplinary preconception counseling due to the high risk of possible uteroplacental complications from the long-term effects of pelvic radiation leading to poor maternal and pregnancy outcomes as no documented pregnancy has successfully occurred with history of >45 Gy prior to this case report.

2. Case report

A 34-year-old G4P2012 with a past medical history significant for Stage III-T3N1M0 anal cancer treated with chemo-radiation and two prior cesarean sections presented at 5 weeks gestation with vaginal spotting after undergoing a frozen embryo transfer of a donor oocyte. She was diagnosed with anal cancer 3 years prior this pregnancy. At the

time of her cancer diagnosis, she was 8 weeks pregnant in her G3 pregnancy. She underwent a laparoscopic ovarian transposition and a dilation and curettage with termination of the pregnancy given the need to move forward with definitive treatment of her anal cancer. She underwent concurrent chemoradiation therapy (5 fluorouracil and mitomycin C) on clinical trial with a proton therapy protocol. The tumor was 7 cm in size with several perirectal lymph nodes that were suspicious for metastatic involvement. Her tumor was treated to 54 Gy in 30 fractions to the high dose region and 45 Gy in 30 fractions to the suspicious lymph nodes. She successfully completed treatment and was in remission for approximately 3 years prior to pursuing reproductive technologies with a successful frozen embryo transfer with a donor oocyte. Prior to undergoing reproductive assistance, the patient was cleared for pregnancy by an outside Maternal Fetal Medicine provider in which records were not available.

At 5 weeks gestation in her G4 pregnancy, she was diagnosed with a subchorionic bleed after presenting with vaginal bleeding. On sonogram at 12 weeks gestation a complete previa was visualized with no clear demarcation between the myometrium and placenta. She was counseled at this visit by MFM that abnormalities associated with the placenta at

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this gestational age were concerning for a placenta accreta. A follow up anatomy scan at 18 weeks and a MRI for placental evaluation was recommended. Risks associated with history of pelvic radiation including fetal growth restriction, placental abnormalities, preterm birth, still birth, and fetal death were discussed at this visit. At 17w6d formal anatomy ultrasound resulted in a normal comprehensive survey. However, a short cervical length of 1.97 cm with a complete placental previa was observed. The myometrial interface appeared to be normal with a small chorion/amnion separation.

She represented at 19w2d with spontaneous vaginal bleeding. On evaluation, a small amount of blood was noted in the vaginal vault. Ultrasound revealed a cervical length of 1.3 cm. Multiple placental lakes and an abnormal interface of the placenta and decidual area of the uterus were seen. On fetal MRI the cervix was measured to be 7 mm in length and 7 mm dilated with protrusion of the placental tissue through the cervix. A placenta increta at the left anterior aspect of the lower uterus, complete placental previa and a small subchorionic hemorrhage measuring 1.8 cm by 0.7 cm were also noted (Fig. 1). These findings were discussed with the patient in a multi-disciplinary care conference involving MFM, Gynecology Oncology, Anesthesia and Radiology. Recommendations at this time were for hospital admission when the patient would desire fetal intervention, sparing no other complications arose, and expectant management if possible until 32 weeks. She was also counseled on cesarean hysterectomy, risks of emergent cesarean hysterectomy and fetal loss. The patient expressed her desire for no fetal intervention until 24 weeks gestation.

At 22w6d gestation, the patient experienced a larger vaginal bleed

and contractions with a quantitative blood loss of 177 cc. A cervical venous sinus was noted on physical examination to be bleeding significantly. The multi-disciplinary team was notified of the change in clinical status, and the recommendation was made to proceed with hysterectomy given the continued bleeding and risk of uncontrolled hemorrhage. At 23w0d, the patient underwent gravid hysterectomy. Intraoperative findings were significant for bladder adhesions to the anterior lower uterine segment with large tortuous vessels. The operation had an estimated blood loss of 2L with no other complications. Photo documentation of intraoperative findings is shown below in Fig. 2. She was resuscitated intraoperatively and transferred post-operatively to the surgical intensive care unit (SICU) for further resuscitation and monitoring. On post-operative day one she was transferred out of the SICU and was subsequently discharged on post-operative day 2. Upon pathological review, the placenta was noted to replace nearly the entire thickness of the myometrium and involve the endocervix consistent with a placenta previa with increta.

3. Discussion

Cervical, anal, or colorectal cancers frequently occur in individuals who are of reproductive age and treatment typically includes radiation (American Cancer Society, 2011; Howlander et al., 2009). Depending on the location and type of cancer at diagnosis, the uterus may be within the target region. The intensity of radiation applied or dosage can result in different short term or long-term effects. Short term effects include diarrhea, pain and/or skin changes, whereas, long term effects include

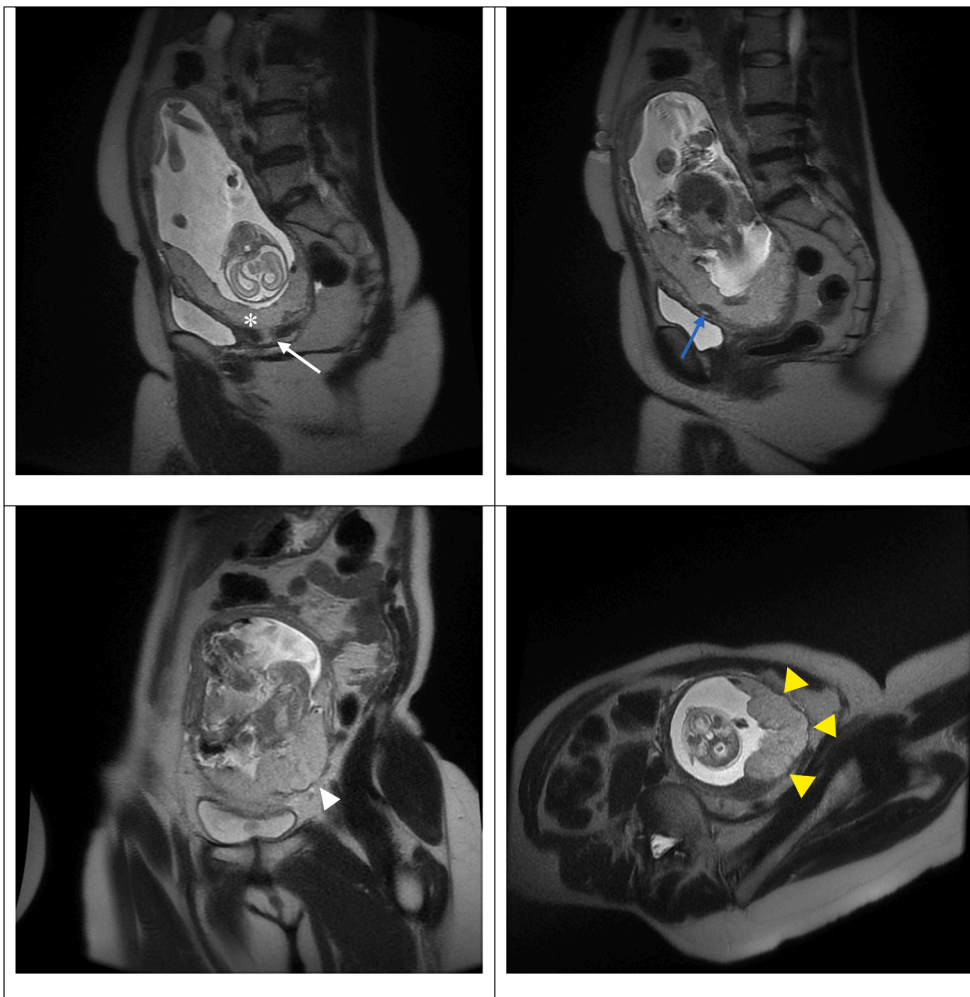


Fig. 1. (Documented as A-D from left to right): A) Sagittal T2-weighted image demonstrates placenta previa (asterisk) with thinning of the cervix and protrusion of the placenta into the cervical canal. B) Parasagittal T2-weighted image demonstrates focal crescentic T2 hypointense signal anteriorly at the placental-myometrial interface (blue arrow) likely representing a small amount of subchorionic hemorrhage. C) Coronal T2-weighted image demonstrates marked thinning of the myometrium with discontinuity along the left inferolateral aspect suggestive of placenta percreta (white arrowhead). D) Oblique axial T2-weighted image demonstrates marked thinning and lobulation of the placental-myometrial interface (yellow arrowheads).

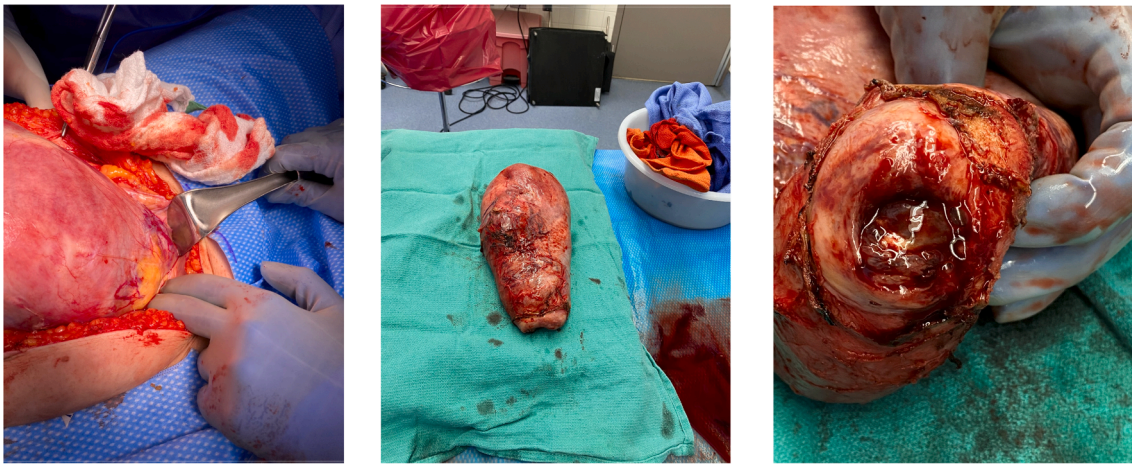


Fig. 2. A) Midline vertical incision exposing the uterus. B) Specimen after removal. C) Dilated cervix with exposed placenta.

scar formation, atrophy and sclerosis (Kurman and Norris, 1977). Specific uterine changes that occur from radiation include an atrophied myometrium and fibrosis of the submucosa leading to decreased uterine volume (Arrive et al., 1989).

With regards to the intensity of radiation, irreversible damage to the uterus has been seen in children who have received 25 Gy. Radiation dosages of < 4 Gy have not been shown to cause any significant changes or impact to fertility (Larsen, 2004; Sudour et al., 2006). The ovaries however, experience irreversible damage at lower dosages of radiation ranging from 12 Gy to 15 Gy (Pridjian et al., 1990). Due to this, ovarian transposition can be offered to patients for ovarian preservation for the intent to prevent the patient from experiencing premature ovarian insufficiency.

Currently, no documented successful pregnancy has been seen in patients who have received > 45 Gy in pelvic radiation. Dosages of 12 Gy have been associated with risks of preterm labor, fetal growth restriction, and miscarriage. The pathophysiology behind these risks, are mainly associated with the long-term changes to the uterus. Fetal growth restriction has been associated with the impaired vasculature of the uterus, whereas myometrial fibrosis has been associated with preterm labor due to decreased uterine volume (Teh et al., 2014). Cervical insufficiency, a cause of preterm labor, has also been a reported outcome of prior pelvic and abdominal radiation. Bowman et al reported of a 23 yo with prior radiation in childhood of 10.8 Gy who was diagnosed with cervical insufficiency at 20 weeks'. She subsequently delivered at 21 weeks due to the inability to perform cervical cerclage. After an abdominal cerclage was placed she was able to carry a future pregnancy until 37 weeks in which she had a cesarean hysterectomy for placenta accreta. Upon pathological examination, no cervical tissue was found.

Other complications that can arise with a history of pelvic radiation is placental abnormalities at a very early gestational age leading to further complications including uterine rupture. This has been reported at gestational ages of 13 and 17 weeks respectively. In both of these cases, the patients presented with severe abdominal pain and hemodynamic instability prompting immediate surgical intervention (Pridjian et al., 1990; Norwitz et al., 2001). These cases that are described above are summarized in Table 1 below.

With known long-term changes to placental vasculature and volume by radiation, studies were performed to determine if these changes can be noted by ultrasound or MRI. In a study of 80 women who received radiation in childhood, a significant uterine volume decrease was observed by ultrasound. Regardless of ovarian conservation or not, a significant decrease in uterine volume was observed (Larsen, 2004). MRI studies were also completed to determine changes to the myometrium and endometrium after radiation. In this study, decreased signal intensity and thickness of the of the myometrium and endometrium were

Table 1

Review of published cases regarding pregnancy complications with prior radiation.

| Gestational Age | Amount of Pelvic or abdominal radiation | Complications |
|--|--|---|
| G1 Pregnancy: 20 weeks (Bowman et al., 2014) G2 Pregnancy: 37 weeks G3 Pregnancy: 37 weeks | 10.8 Gy in abdominal and pelvic radiation (Bowman et al., 2014). | G1: Cervical insufficiency leading to preterm delivery G2: Abdominal cerclage leading to planned cesarean section at 37 weeks with very thin lower uterine segment. G3: Placenta accreta requiring cesarean hysterectomy (Bowman et al., 2014). |
| G1 Pregnancy: 13 weeks (Pridjian et al., 1990) G1 Pregnancy: 17 weeks (Norwitz et al., 2001) | 7000 rad external beam radiation (Pridjian et al., 1990). 875 rad total body irradiation in a single dosage (Norwitz et al., 2001). | G1: Uterine rupture with placental inacta on pathology (Pridjian et al., 1990). G1: Uterine rupture with placental percreta (Norwitz et al., 2001). |

found. This signal decrease on the T2 images signified atrophy and fibrosis of these layers (Arrive et al., 1989). However, even though these changes can be seen on imaging, there are no current guidelines for how to use these screening tools for pre-conception counseling.

Due to the long-term changes to the vascularity and volume of the uterus from radiation, methods into reversing these changes has been researched. One method was to determine if uterine volume and endometrial thickness responded to physiological sex steroid replacement of estradiol patches and vaginal progesterone pessaries. Improvement in uterine volume was documented but no significant change in uterine blood supply or endometrial thickness was noted (Bath et al., 1999). Similar to the previous, another study investigated sex steroid replacement of women who received abdominal radiation in childhood with radiation induced ovarian insufficiency. These individuals were treated with physiological sex hormone replacement with no change in uterine blood flow or endometrial thickness, suggesting that uterine radiation damage is irreversible (Critchley et al., 1992). Regardless of these outcomes, no studies have been completed to determine if preconception treatment with sex steroid replacement will improve pregnancy outcomes.

Based on prior studies and this particular clinical outcome, counseling dependent upon the duration, intensity and age at which the patient received radiation needs to be completed. Currently there is no documented successful pregnancy in a patient with > 45 Gy in pelvic radiation with this being the furthest documented. With no current

recommended screening methods for uterine volume or vascularity and no recommended treatment for reversing the effects of uterine radiation, the risks associated with proceeding with attempted pregnancy are high. There are also no specific guidelines for preconception evaluation in patients with pelvic radiation history with current recommendations for pre-treatment consultation to Reproductive Endocrinology and Infertility for oocyte preservation if possible. Patients with a history of receiving high doses of pelvic radiation should be counseled against attempting pregnancy due to these risks and the high risk of possible uteroplacental complications from the long-term effects of pelvic radiation leading to poor maternal and pregnancy outcomes. With any history of pelvic radiation regardless of dosage, delivery counseling should include discussion regarding possible cesarean hysterectomy as this has a higher morbidity and mortality rate than other deliveries and may be needed for obstetrical indications including placenta accreta, percreta etc. Treatment of these pregnancy complications requires a multi-disciplinary team involving maternal fetal medicine, radiology, gynecology oncology, anesthesia, and neonatology.

4. Consent

“Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.”

CRediT authorship contribution statement

Amanda Baucom: Writing - original draft. **Thomas Herzog:** Writing - review & editing. **Amanda Jackson:** Writing - review & editing. **Shaun A. Wahab:** Visualization, Writing - review & editing. **Caroline Billingsley:** Supervision.

Declaration of Competing Interest

Caroline Billingsley reported of two conflicts of interest. She has received payment or Honoraria for a lecture on ovarian cancer and she

currently serves on the Disease Safety Monitoring Board at the University of Cincinnati. No other conflicts of interest were disclosed from other authors.

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