A fight-and-flight for life: A rare case of advanced cervical cancer in pregnancy

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A R T I C L E  I N F O

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A B S T R A C T

Background: Advanced cervical cancer during pregnancy is an extremely rare event. We describe a case of at least stage IIIB cervical squamous cell carcinoma during pregnancy. This may possibly represent the longest gestation from time of diagnosis to delivery in a case of advanced cervical cancer, with potentially the most advanced gestational age at delivery and a relatively favorable outcome in the current literature.

Case: A 29-year-old female at 20 0/7 weeks of gestation with at least stage IIIB squamous cell carcinoma of the cervix flew from Micronesia to Hawaii for oncologic treatment. After consultation with gynecologic oncology and maternal-fetal medicine, she opted to continue the pregnancy and began neoadjuvant chemotherapy with carboplatin and paclitaxel. At 33 2/7 weeks of gestation, she was admitted for preterm prelabor rupture of membranes and immediately underwent a cesarean delivery for heavy vaginal bleeding. Postpartum, she underwent cisplatin chemotherapy with concurrent radiation therapy. After 6 cycles of chemotherapy, the patient’s cancer had progressed to the point that hospice was recommended. She died 11 months after initial presentation.

Conclusion: Advanced cervical cancer during pregnancy requires individualized treatment, shared decision making, and a multidisciplinary team approach. If the pregnancy is continued, antepartum chemotherapy should be strongly considered. Maternal prognoses tend to be poor, but neonatal outcomes appear to be favorable.

1. Introduction

Cervical cancer is the leading cause of cancer-related deaths in women worldwide, with approximately 300,000 deaths each year (National Institute of Health, 2020). However, invasive cervical cancer during pregnancy is an extremely rare event, with an incidence between 0.05% and 0.1% (La Russa and Jeyarajah, 2016). Management of invasive cervical cancer during pregnancy is particularly challenging and requires a multidisciplinary team, including gynecologic oncology, maternal-fetal medicine, and neonatology. Most documented cases of cervical cancer during pregnancy are diagnosed as early stage cancers, and maternal outcomes have been found to be similar to those of nonpregnant women (La Russa and Jeyarajah, 2016; Bigelow et al., 2017; Van Der Vange et al., 1995).

Little is known about maternal and fetal outcomes of advanced cervical cancer diagnosed during pregnancy, especially for patients who decide to continue the pregnancy. To date, only a few case reports have been published on at least stage IIIB cervical squamous cell carcinoma (SCC) in patients who desired continuation of pregnancy. We present a rare case of at least stage IIIB cervical SCC in pregnancy, in addition to reporting possibly the longest gestation from time of diagnosis to delivery and possibly the most advanced gestational age achieved at delivery with a relatively favorable outcome in the current literature.

2. Case presentation

A 29-year-old, gravida-4 para-3 female at 20 0/7 weeks of gestation presented to the Emergency Department for back pain and right leg numbness. The patient had been diagnosed with cervical cancer at her initial prenatal appointment in Micronesia and had recently flown to Hawaii with the intention of finding a provider who could manage her cancer. Pelvic exam revealed a large fungating gray mass that encompassed the entire cervix and a firm nodular tumor that was fixed to the right pelvic sidewall, extending distally to the the vagina. The mass was biopsied with minimal blood loss, and pathology resulted as invasive SCC, poorly differentiated (Fig. 1). Computed tomography (CT)
of the abdomen and pelvis was significant for a cervical mass with focal extension into the parametrial fat (3.7 × 2.5 cm), invasion of the urinary bladder with obstruction of the distal right ureter, moderate right hydronephrosis, and a necrotic right pelvic sidewall lymph node (2.3 × 1.7 cm) suggestive of malignant nodal spread (Fig. 2). CT of the chest was negative for metastasis. Positron emission tomography (PET) was deferred since pregnancy is a contraindication. The patient was admitted for pain control and placement of a right ureteral stent for obstructive hydronephrosis secondary to the tumor burden.

The following day, a multidisciplinary meeting was held with gynecologic oncology, maternal-fetal medicine, neonatology, family planning, critical care, palliative care, and social services. The patient was counseled extensively about her diagnosis of at least stage IIIB cervical SCC based on the 2018 International Federation of Gynecology and Obstetrics Staging System and the risks and benefits of terminating versus continuing the pregnancy; she strongly desired to continue the pregnancy. She was discharged from the hospital with plans to start outpatient neo-adjuvant chemotherapy with carboplatin area under the curve of 6 mg/mL·min every 3 weeks and paclitaxel 175 mg/m² every 3 weeks and to anticipate delivery at 34 0/7 weeks of gestation via cesarean delivery.

After the initiation of chemotherapy, the patient appeared to clinically improve. The tumor began to decrease in size on physical exam and her pain gradually improved. She received a total of 4 cycles of chemotherapy. Her pregnancy course was complicated by chronic hypertension that was controlled on nifedipine 60 mg daily and labetolol 200 mg twice daily as well as gestational diabetes, well controlled on metformin 500 mg twice daily. Interval ultrasounds showed normal fetal growth.

At 33 2/7 weeks of gestation, the patient presented to Labor and Delivery for preterm prelabor rupture of membranes and heavy vaginal bleeding. Given the amount of bleeding, she underwent an urgent primary cesarean delivery prior to her anticipated delivery at 34 0/4 weeks of gestation, with a fundal hysterotomy to maximize the distance between the hysterotomy and anticipated site of pelvic radiation therapy. The infant was delivered with Apgar scores of 8 and 9 at 1 and 5 min, respectively, and weighing 2120 g. Intraoperatively, enlarged pelvic lymph nodes were palpated bilaterally. Otherwise, there was no evidence of disease on the uterus, bladder, rectum, liver, or diaphragm. The patient was discharged home on postoperative day 3.

Postpartum, magnetic resonance imaging showed doubling in size of the partially necrotic pelvic mass (8.1 × 6.9 × 7.2 cm) with extension along the sacral roots and a new cystic mass (5.5 × 4.3 × 6.3 cm) along the right iliac region likely representing a metastasis (Figs. 3 and 4). PET showed no evidence of disease beyond the pelvis. At 6 weeks postpartum, the patient had fully recovered from her cesarean delivery and started weekly cisplatin with concurrent radiation therapy. After 6 cycles of cisplatin, repeat pelvic exam revealed an enlarging tumor and necrotic friable tissue on the right pelvic sidewall. Repeat PET showed a 10.9 × 8.5 × 4.8 cm heterogeneous necrotic mass in the pelvis extending to and involving the uterus, bladder, right ureter, rectosigmoid colon, and sacral neural foramina. Given the absence of good treatment options, the recommendation was made to the patient to return home to Micronesia so that she may spend time with her children and family. She declined hospice at this time.

Two weeks later, the patient presented to the Emergency Department for heavy vaginal bleeding. In the Emergency Department, she lost consciousness and went into cardiopulmonary arrest. Resuscitative efforts led to return of spontaneous circulation in 10 min,
and she was transferred to the intensive care unit intubated and receiving blood products. The patient was stabilized and extubated after 2 days. She was discharged home on hospital day 8 and flew back to Micronesia. Three months later, her family sent a letter that she had died at home, which was 8 months postpartum and 11 months after her initial presentation to the Emergency Department.

3. Discussion

Advanced cervical cancer in pregnancy is a very rare event, and to date, only a few case reports have been published on patients with at least stage IIIB cervical SCC and continuation of pregnancy (Table 1). Advanced cervical cancer in pregnancy represents a medical dilemma because both known literature and treatment options are limited.

Management of cervical cancer in pregnancy is based on extent of disease burden, gestational age, patient’s desire to continue or terminate the pregnancy, and state laws regarding termination of pregnancy. Various evidence-based guidelines have been developed for the management of early cervical cancer in pregnancy. However, the management of advanced cervical cancer in pregnancy is predominantly based on theory and expert opinion due to a lack of large databases, prospective trials, and randomized controlled trials.

In the absence of evidence-based treatment algorithms, informed consent and shared decision making are essential when creating an individualized patient-centered management plan. Providers must remain objective and nonjudgmental when counseling patients, and a multidisciplinary team approach will optimize patient care given the complexity of such cases. If a facility is unable to provide adequate resources, such as this patient from Micronesia, then referral to a capable center is crucial.

If a patient opts to continue the pregnancy, the safety of intentionally delayed treatment, as proven in early cervical cancer (La Russa and Jeyarajah, 2016; Bigelow et al., 2017; Amant et al., 2009; Hecking et al., 2016; Kohler et al., 2015; Zagouri et al., 2013), is difficult to assess in advanced stages. Experts strongly recommend the initiation of neoadjuvant platinum-based chemotherapy to prevent cancer progression while awaiting fetal maturity (La Russa and Jeyarajah, 2016; Bigelow et al., 2017; Amant et al., 2009; Hecking et al., 2016; Kohler et al., 2015; Zagouri et al., 2013). Ideal regimen and dosing are unknown.

Platinum crosses the placenta and is found at lower concentrations in the umbilical cord (23–65%) and amniotic fluid (11–42%) than maternal blood (Kohler et al., 2015). Chemotherapy is contraindicated in the first trimester due to risk of abortion and major fetal malformation during organogenesis (Zagouri et al., 2013; Cardonick and Iacobucci, 2004). After completion of the first trimester, teratogenic effects appear to be minimal. A systematic review and meta-analysis of platinum-derivatives during pregnancy found 67.4% completely healthy neonates (Zagouri et al., 2013). Neonatal complications included respiratory syndrome disorder (14.6%), intraventricular hemorrhage (2.1%), anemia (2.1%), mild elevation in creatinine (2.1%), and hypoglycemia (2.1%) (Zagouri et al., 2013). At 12 months, all offspring were reported healthy, but the long-term effects of in utero chemotherapy have yet to be determined (Zagouri et al., 2013).

Antepartum complications seem to be infrequent, with the most common being iatrogenic preterm birth to facilitate oncologic treatment (Bigelow et al., 2017). Hypertensive disorders should also be noted. Behaim et al. described a patient with stage IIIB cervical SCC that underwent 2 cycles of antepartum cisplatin and delivered a healthy neonate at 28 weeks of gestation for preeclamptic syndrome (Behaim et al., 2008). Similarly, our patient developed hypertension with proteinuria. Maternal-fetal medicine diagnosed her with chronic hypertension and tumor-induced proteinuria due to renal involvement, and her blood pressures were controlled with antihypertensive medications. Distinguishing between preeclampsia, tumor-induced hypertension and proteinuria, and cisplatin nephrotoxicity can be subtle but is very important in determining patient management and allowing for fetal maturation, especially when very preterm.

The patient described by Behaim et al. was delivered at an earlier...
gestational age and was able to initiate postpartum chemoradiation therapy earlier than our patient, who delivered at 33 weeks of gestation. The patient survived for 10 months after her diagnosis of cervical cancer, which was similar to our patient at 11 months. Despite an earlier initiation of chemoradiation, maternal prognosis was similar to our patient, and our fetus likely benefited from additional time to gestate. Therefore, in the absence of routine obstetrical indications, delayed delivery with neoadjuvant chemotherapy is a reasonable option.

The literature describes two other case reports of at least stage IIIB cervical SCC in pregnancy. In Takushi et al., a patient was delivered one week after being diagnosed with IIIB cervical SCC at 30 weeks of gestation and survived for 4 months (Takushi et al., 2002). In Marnitz et al., a patient with IVB cervical SCC underwent 12 weeks of neoadjuvant chemotherapy and delivered a healthy neonate at 32 weeks of gestation, which was comparable to our patient’s 13 weeks of delayed delivery (Marnitz et al., 2010). Unfortunately, maternal outcome for that patient is unknown, which highlights a lack of knowledge in this particular area of medicine. Our case could represent possibly the longest delayed delivery and possibly the most advanced gestational age achieved at delivery with a relatively favorable outcome in the current literature. However, each patient must have an individualized treatment plan, and without adequate data, we have yet to determine the best management for patients with advanced cervical cancer in pregnancy.

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Declaration of Competing Interest

The authors have no actual or potential conflicts of interest.

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