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Case report

Vaginal cancer diagnosed in the second trimester of Pregnancy: The impact of current abortion law on cancer care in Louisiana

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1. Introduction

Primary vaginal cancer is a rare disease. According to the American Cancer Society, there are an estimated 8,870 new cases of vaginal and other female genital cancers in 2022 (American cancer society cancer statistics center. https://cancerstatisticscenter.cancer.org/_ga=2., 2018). Most primary vaginal cancers are HPV-associated squamous cell carcinoma; however, adenocarcinoma, sarcoma, and melanoma of the vagina can also occur. The Society of Gynecologic Oncology identifies risk factors for vaginal cancer as HPV infection, age > 60, and vaginal precancerous lesions, cervical cancer, smoking, HIV, autoimmune conditions, or any other immunosuppressing condition (Va, xxxx). The most common symptom is vaginal bleeding, but many patients are asymptomatic. Poor prognostic factors for primary vaginal cancer include advanced FIGO stage, tumor size > 4 cm, tumor involvement of the entire vagina, and lymph node metastasis (Yang et al., 2020).

Due to the rarity of this disease, there are no randomized controlled trials detailing a treatment algorithm for vaginal cancer and it is the only primary gynecologic malignancy without treatment guidelines published by the National Comprehensive Cancer Network (NCCN). As such, most of the treatments have been adapted from the approach to cervical cancer. For stage I and stage II primary vaginal cancer, surgical management has been shown to be equally effective as primary radiation treatment (Yang et al., 2020). Surgical management can include radical hysterectomy, radical vaginectomy, bilateral salpingectomy, and pelvic lymphadenectomy. Ovarian preservation is preferred in pre-menopausal patients to prevent surgical menopause. Vaginal cancer diagnosed in pregnancy is even more rare, and delays in treatment to prolong pregnancy are associated with disease progression and poor prognosis (Samejima et al., 2021). With informed consent from the patient, we present a case of a 35-year-old female with stage I primary vaginal cancer diagnosed in her second trimester of pregnancy and the complex multi-disciplinary treatment she subsequently underwent to treat this rare and potentially aggressive disease.

In the background of this patient's diagnosis, legal restrictions on abortion were in flux nationally. On June 24, 2022, the United States Supreme Court ruled on Dobbs v. Jackson Women's Health Organization and decided that there is no constitutional right to abortion in the United States (Dobbs v. Jackson Women's Health Organization, 597 U.S. 2-78, 2022). This overturned the precedent set by Roe v. Wade in January of 1973. In overturning Roe, the Dobbs decision, which eliminated federal protection for abortion rights in the United States. Immediately following the Supreme Court decision, a Louisiana "trigger law" went into effect, making abortion illegal in the state. A temporary restraining order was granted on June 27th, but on July 8th, the ban went back into effect (Kask, (2022, July 1).). On July 12th, the ban was again blocked, however, on July 29th the state appeals court ruled that the abortion ban must be upheld while the legal challenges are resolved.

Prior to Roe being overturned, Louisiana laws on abortion care changed often and were consistently tightened to limit patient's access to abortion. In the time frame immediately preceding the Dobbs decision, abortion care in Louisiana was limited to pregnancies under 22 weeks gestation. There was also a "dismemberment bill" passed in 2016 that prohibited the dilation and evacuation (D&E) procedure if a pregnancy was 15 weeks or beyond and there was a heartbeat present in the fetus (Johnson, 2016). This law was not enforced while it was fought through the legal system but went into full effect in April 2022.

2. Case Report

A 35-year-old G2P2002 with no prior history of lower genital tract dysplasia or immunosuppression presented for routine well-woman care at an indigent care clinic affiliated with the Catholic church. Due to this affiliation with the church, contraception services are not offered. Her

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routine pap smear showed high grade squamous intraepithelial lesion (HSIL), HPV +. The patient subsequently had a colposcopy with a biopsy that revealed high grade cervical dysplasia (CIN3). There were no vaginal abnormalities noted on this examination. She was uninsured and was referred to a large tertiary care center with the capability to provide financial aid for surgery. At her pre-operative visit, she was noted to have a positive pregnancy test, which the patient reports was unplanned but desired. The patient, now a G3P2002, underwent repeat colposcopy with cervical biopsies which were reported as "focally denuded transformation zone mucosa with marked chronic cervicitis and focal squamous atypia.".

In the setting of CIN3 in pregnancy, gynecologic oncology was consulted for a second opinion. At her initial gynecologic oncology visit the patient was 14w4d. She denied pelvic pain or vaginal bleeding. On physical exam, she was found to have a friable 1.5 cm mass in the posterior upper vagina in the midline, which had not been previously described. Biopsies of this vaginal mass showed invasive poorly differentiated squamous cell carcinoma.

A pelvic MRI was obtained to evaluate the extent of disease spread, which revealed only the mass in the posterior upper vagina with no parametrial invasion and an incidental finding of a large calculus in a left ureterocele with hydronephrosis (Fig. 1). There was no pelvic lymphadenopathy. The patient was counseled on options for cancer treatment, including definitive surgical management and primary chemoradiation. It was reviewed with the patient that there is limited data for the treatment of vaginal cancer, and even less data detailing the treatment of vaginal cancer in pregnancy. Based on available evidence and given that size of the mass was < 2 cm and limited to the upper vagina, she was recommended to undergo primary surgical resection to treat her cancer. After extensive counseling and using shared-decision making, the patient decided to proceed with termination of pregnancy followed by radical hysterectomy, upper vaginectomy, bilateral salpingectomy, and bilateral pelvic lymphadenectomy.

She was induced at 16 weeks with high dose misoprostol and her delivery was overall uncomplicated. Following termination of pregnancy, she underwent a CT chest/abdomen/pelvis that showed no evidence of metastatic disease and an incidental left ureterocele causing left sided hydronephrosis. Within 2 weeks of termination of pregnancy, she underwent radical abdominal hysterectomy, upper vaginectomy, bilateral salpingectomy, and pelvic lymphadenectomy. Intra-operative findings revealed the midline upper vaginal mass, an enlarged 15–16 cm uterus with a normal appearing cervix and normal appearing intra-abdominal structures. She did have left-sided hydronephrosis with a ureter dilated to 1.5 cm and a nodule was palpable in the bladder, consistent with her pre-operative imaging. Pathologic evaluation revealed a 2.2 cm ill-defined, friable and ulcerated mass in the posterior vaginal wall of the resection specimen (Fig. 2). Microscopically, HPV-associated poorly differentiated squamous cell carcinoma was noted, comprising of focal poorly differentiated conventional squamous cell carcinoma, in association with nests of large undifferentiated cells in a distinctive chronic inflammatory background, with features of lymphoepithelioma like carcinoma (Fig. 3). The carcinoma was confined to the vaginal wall, with negative margins and lymph nodes (pT1b, N0, M0). The invasive carcinoma was 2 mm from the posterior margin. Due to this close posterior margin, the patient was offered adjuvant radiation. After a discussion of risks and benefits, decided to proceed with close observation.

3. Discussion:

Primary vaginal cancer is a rare diagnosis, and cancer diagnosed in pregnancy is even rarer. One literature review described only 12 reported cases of primary invasive vaginal cancer diagnosed during pregnancy (Korenaga and Tewari, 2020). The patient was counseled about her options for treatment using the limited research available. One literature review showed that patients with stage I disease treated initially with surgery had a mean 5-year survival rate of 77%, regardless of whether adjuvant radiation treatment was administered (Tjalma et al., 2001). Surgery alone as a treatment modality is associated with the lowest risk of mortality (Shah et al., 2009). The patient was also counseled that treatment for her cancer would be incompatible with pregnancy. She decided to terminate the pregnancy and pursue surgical treatment for her cancer, but because this patient's cancer diagnosis arrived in the middle of a contentious legal battle over abortion care, her options for termination were limited. Due to the "dismemberment bill" this patient could only be offered an induction of labor for termination, even though induction of labor has a much higher complication rate, with an adjusted risk ratio of 8.5 when compared with D&E (Bryant et al., 2011).

Case reports of vaginal cancer in pregnancy have described mixed outcomes, however, intentional delays in treatment to prolong pregnancy have been shown to have deleterious consequences. One such patient at 13 weeks gestation was found to have stage 1 vaginal cancer diagnosed following transvaginal tumor resection. The recommended treatment was radical surgery following termination, however the patient opted against surgery due to desire to preserve the pregnancy. At 22 weeks, the patient was found to have a progression of disease with a large invasive mass and was induced at 26 weeks with plans to start chemoradiation. She could not tolerate chemotherapy and was treated with radiation alone, but later developed lymph node metastases and died 8 months after delivery (Samejima et al., 2021). Clinicians should be mindful of the potential consequences of delays in treatment on long-term survival and morbidity, and these should be clearly discussed with any patient diagnosed with cancer in pregnancy.

Receiving the diagnosis of cancer in pregnancy is dangerous at any time, but even more so in the current anti-abortion climate. In the wake

Fig. 1. Pelvic MRI, high resolution T2 sequence. Sagittal and coronal views.

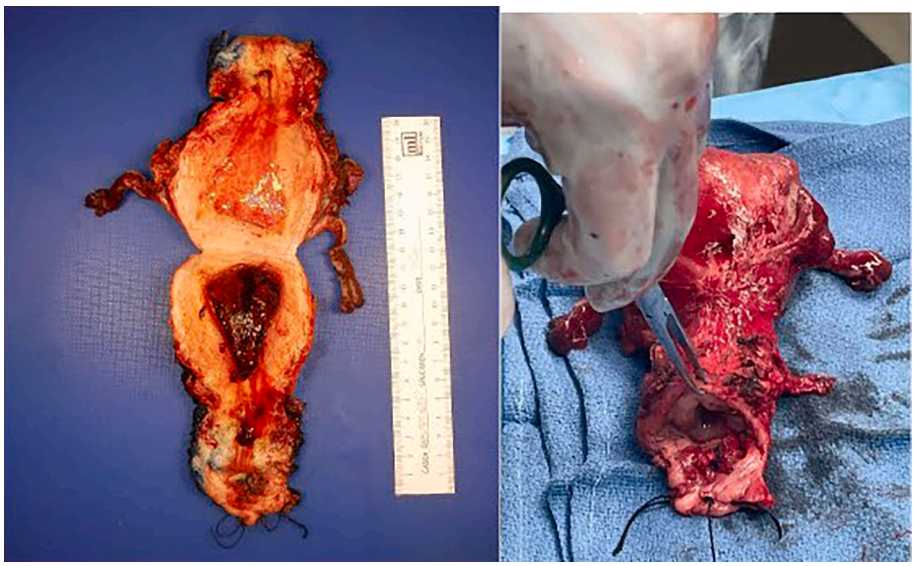

Fig. 2. Uterus, bilateral fallopian tubes, and upper vagina with vaginal tumor.

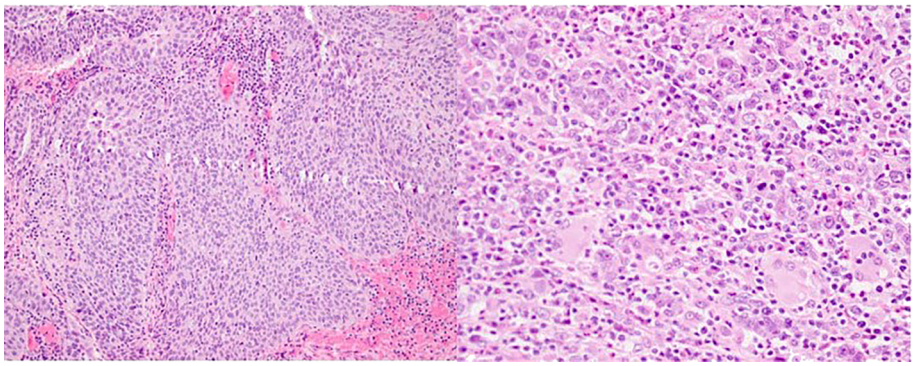

Fig. 3. Conventional invasive squamous cell carcinoma (left) with lymphoepithelioma-like carcinoma (right).

of the Supreme Court decision to overturn Roe v. Wade, many states have passed legislation making abortion illegal. Currently, abortion in the state of Louisiana is allowed only in cases where there is a risk of maternal death or to prevent serious, permanent impairment of a life-sustaining organ. Abortion is also permitted in cases of "medically futile" pregnancies, in which a profound and irremediable congenital or chromosomal anomaly incompatible with sustaining life is present. Many hospitals issued bans on abortion and required consultation with hospital attorneys and ethics committees prior to offering any patient a termination. In cases where the risk to the mother's life is not emergent, this represents an unnecessary delay in care and infringes on the doctor-patient relationship.

Even with the current exceptions present in Louisiana allowing abortion, there is still the "dismemberment bill" which greatly limits the methods abortion providers can offer patients if they are past 15 weeks gestation, even if they have a pregnancy that falls in the parameters of the exceptions outlined in the trigger law. This limits safe and ethical treatment of patients in need of termination of pregnancy. Louisiana patients are not only at greater risk physically, but also emotionally due to the traumatic experience of having only one option for termination past 15 weeks gestation – an induction of labor and delivery of a fetus.

These laws represent a potential barrier to cancer care, and will result in delays in treatment which, as described above, can result in disease progression and increased risk of morbidity and mortality. This case was diagnosed soon after Louisiana passed legislation making abortion illegal, and this patient was able to be counseled and have an induction in the two-week period in which abortion was permitted due to legal challenges to the trigger law. Whether this patient would have been offered expeditious treatment had her cancer been diagnosed even a few weeks later is unknown.

Some patients may be able to pursue alternatives, such as traveling to states with fewer restrictions. However, for many patients this presents a significant financial and logistical barrier. As was the case for our patient, approximately 60% of patients who had abortions in 2020, the most recent year for which the CDC has published data, had at least one prior live birth (Kortsmit et al., 2022). In the dissenting opinion for Dobbs v. Jackson, Justices Stephen Breyer, Sonia Sotomayor, and Elena Kagan remind us that in addition to the costs of travel, lodging, and medical care, patients may also incur the cost of time away from work and childcare (Dobbs v. Jackson Women's Health Organization, 597 U. S. 2-78, 2022). The laws also create a significant fear of legal ramifications for providers. In Texas for example, any person can sue a physician they believe has performed an illegal abortion and may even be financially compensated "in an amount not less than $10,000" if their suit is successful (Hughes, 2021). In Louisiana, providers face the threat of 1–10 years in prison and between $10,000 and $100,000 fines (Senate and No, 2022).

There is limited literature to guide treatment of vaginal cancer in pregnancy. However, reports have demonstrated the rapid progression of disease and dangers of delaying treatment to prolong pregnancy. In this situation, we must consider the four pillars of medical ethics: beneficence, non-maleficence, autonomy, and justice. It was in this

patient's best interest to offer termination of pregnancy and subsequent surgical management. We respected her autonomy in choosing to proceed with this plan and did so without fear of legal ramifications because her case occurred at a time when the law was in flux. However, the principles of autonomy and non-maleficence were infringed upon in this case when the patient was denied the full spectrum of abortion care. In compliance with Louisiana law, she was only offered an induction of labor as opposed to a D&E, despite D&E being a far safer and less traumatic procedure. Limitations on what providers can and cannot offer their patients, whether based on religious restrictions or the law, sets a dangerous precedent that has the potential to harm all patients, especially those seeking cancer care. The first words many of us utter as we begin our journey in medicine are those of the Hippocratic Oath, in which we swear to provide care for the benefit of the sick and do no harm. In seeking justice for our patients, we must remember our oath and advocate for a return to these basic principles.

Conflict of Interest Statement:

Dr. Nair received a one-time honorarium of $500 from the Women's Foundation. She has also received travel support from GOG New Investigators for attending NRG meetings. She is a non-voting member of the Foundation for Women's Cancer board. She is also Vice Chair of the SGO Diversity, Inclusion, and Health Equity Committee. The other authors have no conflicts of interest to disclose.

CRediT authorship contribution statement

Fraya G. King: Conceptualization, Writing – original draft. **Vibha Rao:** Writing – review & editing. **Wenjing Qiu:** Writing – review & editing. **Ritu Bhalla:** Writing – review & editing. **Nicole E. Freehill:** Writing – review & editing. **Navya Nair:** Conceptualization, Writing – review & editing, Supervision.

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.

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