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Case Report

Management of High Risk Pap Smears in Pregnancy: A Case of a Near Miss

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Abstract

Cervical cancer screening should be included during routine prenatal care and the American Society for Colposcopy and Cervical Pathology guidelines should be followed for the management of abnormal cervical cytology. Cervical cancer is the most common gynecologic malignancy diagnosed in pregnancy with treatment varying significantly depending on stage of disease. Diagnostic work-up and treatment of cervical cancer should be provided during pregnancy. We report the case of a 33-year-old G4P3104 who was diagnosed with squamous cell carcinoma of the cervix during third trimester pregnancy. Her first trimester pap smear demonstrated high grade squamous intraepithelial lesion, but no biopsy was performed. Invasive squamous cell carcinoma was identified on third trimester biopsy. Patient underwent Cesarean radical hysterectomy, bilateral pelvic lymphadenectomy, and bilateral oophoropexy followed by adjuvant radiation for International Federation of Gynecology and Obstetrics (FIGO) stage IB2 squamous cell carcinoma of the cervix.

Keywords: Cancer and Pregnancy; Cervical Cancer; Cervical Cancer Screening; Colposcopy

Introduction

Prenatal care involves screening and treatment of medical conditions that affect maternal and fetal health, including infectious diseases, genetic abnormalities, and cervical cancer. Cervical cancer screening is completed via the Papanicolaou (Pap) smear and/or Human Papillomavirus (HPV) testing. A Pap smear involves collection and cytological examination of ectocervical and endocervical cells. Women aged 30-65 should be screened with the addition of HPV co-testing per the American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines. If abnormalities are detected during screening, prompt evaluation and treatment should be performed. In the setting of early-stage cervical cancer, surgical management can be performed at the time of Cesarean section delivery. We report a case of International Federation of Gynecologic Oncology (FIGO) stage IB2 squamous cell carcinoma of the cervix diagnosed during third trimester pregnancy with possible missed opportunity for earlier diagnosis.

Case

A 33-year-old Caucasian, now G4P3104, presented for routine prenatal care. A Pap smear collected at 14w4d demonstrated High Grade Squamous Intraepithelial Lesion (HSIL) with features suggestive of endocervical gland involvement. High risk Human Papillomavirus (HPV) testing was negative. The patient was instructed to follow up in 2-4 weeks for a prenatal visit and colposcopy.

Colposcopy at 16w5d demonstrated acetowhite changes on the cervix at 5-7 o'clock with fine punctations (Figure 1A). No biopsies were obtained at that time, but the impression was noted to be HSIL. Recommendation was made for repeat colposcopy during third trimester, which was performed at 31w5d. Gross

cervical changes were noted with an ulcerative lesion described (Figure 1B). Acetowhite changes, punctuation, mosaicism, abnormal blood vessels, and raised borders were present. Biopsies were taken at 12 o'clock. The colposcopic impression was severe dysplasia. Pathology reported Cervical Intraepithelial Neoplasia 3 (CIN 3). The obstetrician then referred the patient to Gynecologic Oncology for further evaluation given concern for malignancy.

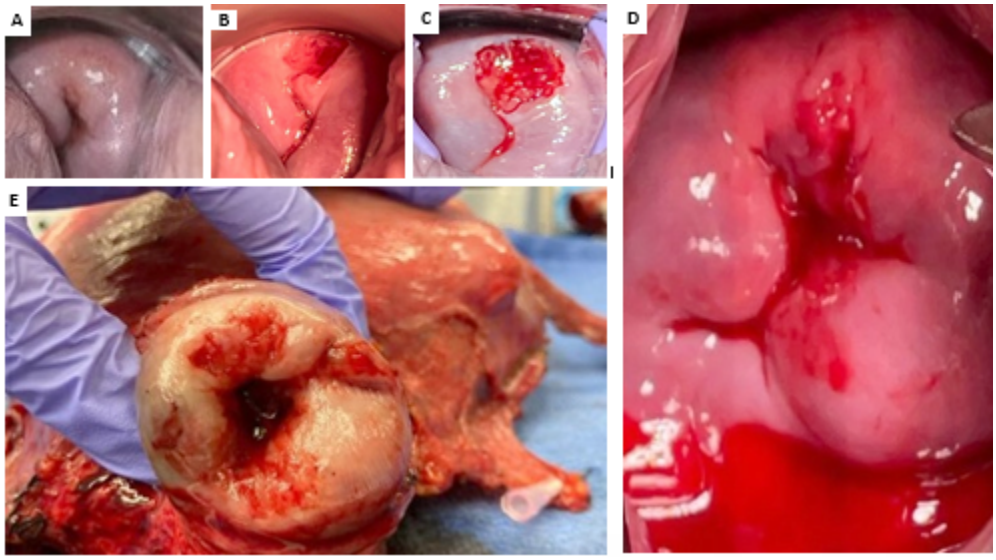

Figure 1: A. Cervix during colposcopy at 16w5d. B. Cervix during colposcopy at 31w5d. C. Cervix at initial gynecologic oncology consultation at 33w2d. D. Intraoperative cervical findings at 36w3d. E. Intraoperative cervical findings after specimen removal.

Upon evaluation by Gynecologic Oncology at 33w2d, there was a 1.5x1.0 cm friable, firm lesion confined to the anterior cervix without extension to vaginal or parametrial tissue (Figure 1C). No supraclavicular or inguinal lymphadenopathy was present on examination. Additional biopsies were obtained and confirmed invasive squamous cell carcinoma.

Positron Emission Tomography/Computed Tomography (PET/CT) was performed and showed no evidence of metastatic disease (Figure 2). Recommendation was made for radical hysterectomy with bilateral pelvic lymphadenectomy and oophoropexy at the time of Cesarean delivery. Maternal Fetal Medicine was consulted for delivery planning. Gynecologic Oncology and Maternal Fetal Medicine agreed to proceed with surgery in the 36th week of gestation after administration of betamethasone for fetal lung maturity.

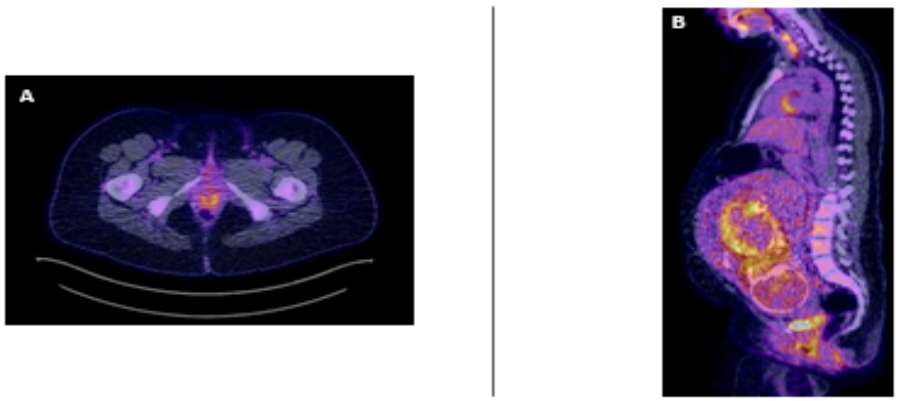

Figure 2: A. Axial PET/CT image. B. Sagittal PET/CT image.

At 36w3d, the patient was taken to the operating room. On pelvic examination under anesthesia, the anterior cervical lesion was 2 cm wide and extended approximately 3cm deep into the endocervical canal (Figure 1D, E). A vertical midline laparotomy was made, and Classical cesarean section was performed without complication for delivery of a viable preterm male infant. Indocyanine green was injected into the cervix after delivery of the infant. We proceeded with attempted sentinel lymph node mapping, modified radical hysterectomy with bilateral salpingectomy, complete bilateral pelvic lymphadenectomy, and bilateral ovarian transposition. Surgery was uncomplicated and she was discharged home on post-operative day 2. Pathology demonstrated invasive moderately differentiated non-keratinizing squamous cell carcinoma of the cervix (Figure 3). The anterior cervical tumor measured 2.3 x 2.2 x 1.1 cm. The depth of stromal invasion was noted to be 11 mm (middle third). Lymphovascular space involvement was detected. The upper vagina, parametria, uterus and bilateral fallopian tubes were uninvolved. All lymph nodes were negative for metastatic cancer. One of the right pelvic lymph nodes was found to have decidualized tissue which was positive for estrogen and progesterone receptors. This histologic finding was further described elsewhere [1]. All margins were negative for invasive carcinoma.

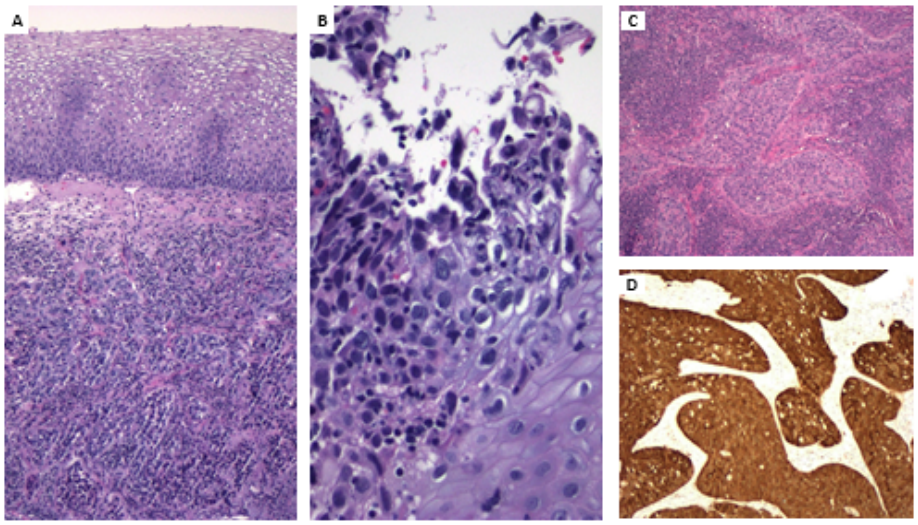

Figure 3: A. Cervical biopsy demonstrating invasive squamous cell carcinoma with overlying benign ectocervical mucosa (H&E 10x). B. Cervical biopsy with squamous cell carcinoma involving the ectocervical epithelium (H&E 40x). C. Hysterectomy specimen with extensive invasive non-keratinizing squamous cell carcinoma (H&E 10x). D. The tumor shows diffuse positivity for p16 (p16 immunostain 10x).

Final stage was International Federation of Gynecology and Obstetrics (FIGO) IB2. The patient was determined to be intermediate risk for recurrence due to tumor size greater than 2 centimeters, middle third stromal invasion, and lymphovascular space invasion. Due to this intermediate risk, adjuvant radiation was recommended to reduce risk of recurrence [2]. Using volumetric modulated arc therapy and CT guidance, 50.4 Gy external beam pelvic radiation was delivered in 28 fractions of 1.8 Gy per fraction over a period of 44 days without unscheduled delays. Completion of treatment was finalized 3 months after surgical management. She has had no evidence of recurrent disease since that time.

Discussion

Cancer in pregnancy has had an incidence of 17-137 per 100,000, specifically 109.1 per 100,000 in the United States [3]. Cervical cancer is the most common gynecologic cancer diagnosed in pregnancy [4], ranging from 1-12 per 10,000 pregnancies [5]. The incidence of pregnancy associated cancers increases as maternal age increases. This has become increasingly significant as many women in the United States are delaying pregnancy for various reasons.

Studies have found that pregnancy may lead to the progression of cervical cancer due to increases in hormones, such as estrogen, progesterone, and HCG [3]. Increases in estrogen can cause both an increase in cervical volume and hypervascularity [6]. The physiologic changes in pregnancy, including a decrease in immunity and an increase in circulation, has been linked to an acceleration in the development of cervical cancer [4].

Pap smear with cervical cytology is the current recommendation for cervical cancer screening. The American College of Obstetricians and Gynecologists (ACOG) recommend

cervical cancer screening starting at age 21. From age 21-29, screening should be completed every 3 years, unless otherwise indicated. From age 30-65, ACOG recommends either cytology every three years, or high-risk HPV and cytology testing every 5 years, or high-risk HPV testing alone every five years [7]. ASCCP guidelines should be followed for the management of abnormal cervical cytology results. Cervical cytology should be collected during pregnancy following with these guidelines. There is no increased maternal or fetal risk for collection of cervical cytology during pregnancy [3].

Abnormal cervical cytology results are commonly found in pregnancy [6]. If a Low Grade Squamous Intraepithelial Lesion (LSIL) is detected on cytology, colposcopy can be completed in the antepartum or post-partum period. Higher grade lesions, such as High Grade Squamous Intraepithelial Lesion (HSIL) and Atypical Squamous Cells Cannot Exclude A High-Grade Lesion (ASC-H) require a colposcopic examination during pregnancy [8]. During pregnancy, endocervical curettage is not recommended [8,9]; however, ectocervical biopsies should be performed if high grade dysplasia or malignancy is suspected. If no lesions or Cervical Intraepithelial Neoplasia (CIN) 1 is identified, the recommendation includes a repeat Pap smear with HPV co-testing in 1 year. If CIN 2-3 is identified, the recommendation includes surveillance colposcopy with repeat co-testing every 12-24 weeks during the pregnancy, however colposcopy can be deferred until the postpartum period [9]. If the clinical appearance of the lesion changes or invasion is suspected, additional colposcopic biopsies would be indicated [9].

If indicated after biopsy, a loop electrosurgical excisional procedure can be completed during the first trimester [6]. Due to increased maternal and fetal risk during the second and third trimester, excisional procedures should be avoided [6]. The importance of biopsy and diagnosis is imperative in the setting of cervical dysplasia or malignancy in pregnancy.

Imaging is important for evaluation of metastatic disease prior to treatment. The patient may be at an increased risk by not completing the imaging studies for diagnosis and staging [10]. Imaging studies which are not associated with a fetal risk are ultrasonography and magnetic resonance imaging without contrast. CT and nuclear imaging modalities can be necessary diagnostic techniques. The radiation dose in these techniques is lower than the necessary dose which causes fetal harm [10]. PET/MRI has been found to be an effective imaging tool for the evaluation of cervical cancer during pregnancy [11,12].

Treatment for cervical cancer varies significantly depending on the stage of disease. The standard treatment recommendation of stage IA2-IB2 cervical cancer is radical hysterectomy with bilateral pelvic lymphadenectomy [13]. Cesarean radical hysterectomy has been found to account for 1% of radical hysterectomies [13]. Oophorectomy at the time of radical hysterectomy should be discussed extensively. Ovarian preservation is commonly recommended given the low incidence of ovarian metastases and the young age at which many cervical cancers are diagnosed. Oophoropexy can be performed if pelvic radiation is indicated.

Conclusion

This case is notable due to early stage of cervical cancer during third trimester pregnancy and possible missed opportunity for earlier diagnosis due to lack of biopsies at the time of colposcopy earlier in pregnancy. This case highlights the importance of cervical cancer screening during pregnancy with colposcopic evaluation and biopsies to further evaluate HSIL or ASC-H. Prompt evaluation and diagnosis of cervical cancer is imperative to determine appropriate treatment plan.

Acknowledgments: None.

Ethical Considerations: Written informed consent was obtained from the patient for publication of the case report.

Conflicts of Interest: None.

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