

CASE REPORT

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Management of cervical cancer in pregnancy in a low resource setting: a rare case report

Namkha Dorji^{1,2*}, Rojna Rai¹, Nishal Chhetri³, Sangay Tshering^{1,2} and Sonam Dechen²

Abstract

Background Cervical cancer in pregnancy is a rare event. Diagnosis and management of cervical cancer in pregnancy is complicated and challenging in a low resource setting.

Case presentation Herein, we present a case of cervical cancer (FIGO stage IB3) diagnosed at 28⁺⁵ weeks and successfully managed at 37⁺² weeks of gestation in a 27-year-old woman.

Conclusion This is the first case report on cervical cancer in pregnancy from Bhutan. It highlights the diagnostic and management challenges in a low resource country.

Keywords Cervical cancer, Cesarean-radical hysterectomy, Pregnancy

Background

Pregnancy complicated with cervical cancer refers to the diagnosis of cervical cancer during pregnancy and up to 6–12 months postpartum period [1]. The incidence of cervical cancer in pregnancy ranges from 0.1 to 12 per 10,000 pregnancies [2].

Cervical cancer in early stage remains asymptomatic, and commonly detected with abnormal screening tests. The symptoms of cervical cancer in pregnancy is similar to non-pregnant women [3]. Pregnancy associated complaints can mask symptoms of cervical cancer, resulting in patients and physicians delay, and higher stages at diagnosis [4]. In a multicenter retrospective study in China, cervical cancer in pregnancy is detected following

bleeding in 85.7%, physical examination in 7.6% and abnormal cervical cancer screening in 6.7% [5].

Any woman presenting with bleeding in pregnancy needs examination and visualization of cervix, and referral to an experienced colposcopist or gynecologist urgently if there is a suspicion of abnormality.

The management of cervical cancer in pregnancy needs to be individualized, and it is dependent on many factors such as gestational age, patient's wishes on continuation versus termination of pregnancy, stage of cancer, availability of neonatal care facilities, and availability of resources for management of cancer [1, 4, 6].

Cesarean-radical hysterectomy had 2.5-fold increased perioperative complication rate as compared with open-radical hysterectomy, increased risk of hemorrhage, increased ileus/small bowel obstruction, but decreased risk of atelectasis, and respiratory failure. There was no difference in the surgical mortality rate between the two groups [7].

To the best of our knowledge, this is the first report of cervical cancer in pregnancy from Bhutan. Herein, we present a case of invasive squamous cell carcinoma of cervix (SCC), grade 2, FIGO stage IB3 in pregnancy in a

*Correspondence:

Namkha Dorji
namji2002@gmail.com

¹Department of Obstetrics and Gynecology, Jigme Dorji Wangchuck National Referral Hospital National Referral Hospital, Thimphu, Bhutan

²Faculty of Postgraduate Medicine, Khesar Gyalpo University of Medical Sciences of Bhutan, Thimphu, Bhutan

³Department of Pathology and Laboratory Medicine, Jigme Dorji Wangchuck National Referral Hospital, Thimphu, Bhutan



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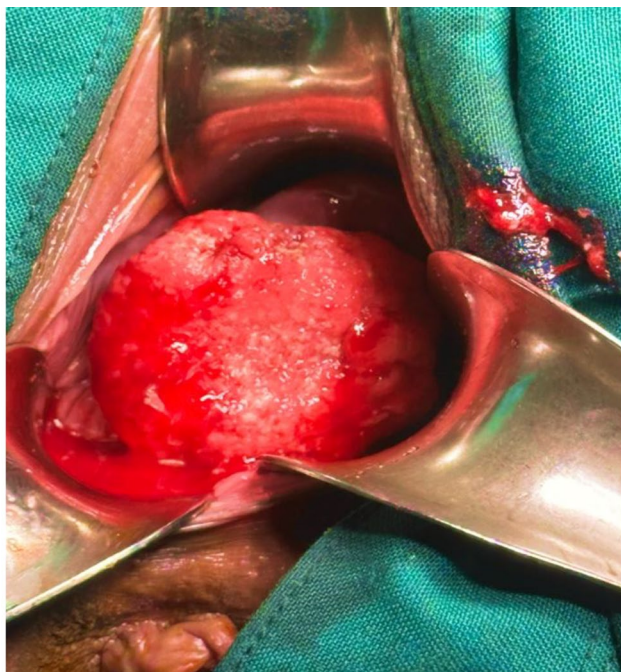


Fig. 1 Huge polypoidal cervical growth with a narrow pedicle arising from 6–9 O'clock position in a 28⁺⁵ weeks pregnant woman

27-year-old woman who initially presented with recurrent antepartum vaginal spotting.

This case report has been reported in line with the Surgical Case REport (SCARE) 2023 criteria [8].

Case presentation

A 27-year-old, gravida-1, para-0, married at the age of 20 years, working in a private firm in Thimphu presented with per-vaginal fresh spotting and lower abdominal pain at 27⁺⁴ weeks of pregnancy. This was a planned pregnancy and the expected date of delivery was confirmed with second trimester dating scan at 15⁺⁴ weeks. Her antenatal screening for human immunodeficiency virus (HIV), hepatitis B, and syphilis were non-reactive. She had menarche at the age of 15 years. Thereafter, her menstrual cycle was regular with 30 days cycle with flow duration of 3–4 days. She didn't have either intermenstrual vaginal bleeding or postcoital bleeding. She is a non-smoker, and she doesn't have significant medical or surgical history. She didn't have sexual partner other than her current husband.

In her first presentation with vaginal spotting, ultrasound scan confirmed a single life fetus, with high anterior placenta without retroplacental clots. Her hemoglobin was 13.30 g/dl, and platelet of 197,000 per microliter. Per-speculum examination was not performed. She was managed conservatively and discharged three days after admission, as the bleeding didn't recur.

However, at 28⁺⁵ weeks of pregnancy, she again presented to the emergency department with similar

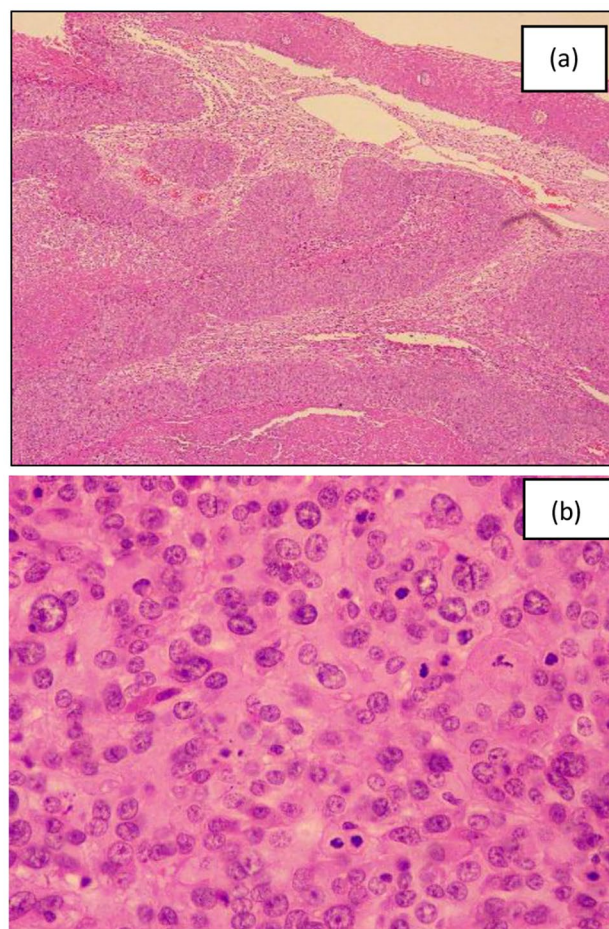


Fig. 2 Microscopic images of the cervical lesion (H&E stain): (a) nest and sheets of infiltrative neoplastic cells with luminal necrosis embedded in desmoplastic stroma (40x); (b) Neoplastic cells with markedly pleomorphic nuclei, vesicular chromatin, prominent nucleoli, eosinophilic glassy cytoplasm and frequent mitoses, including atypical mitosis (400x)

complaints of fresh vaginal spotting. On admission, her vitals were stable and clinically was not pale. Repeat fetal scan was normal. Per-speculum examination revealed a huge friable polypoidal growth (6*6 cm) with contact bleeding with narrow pedicle arising from 6–9 o'clock position of cervix (Fig. 1). She was then admitted to the maternity ward for further diagnostic workup.

After taking a written informed consent, examination under anesthesia with polypectomy (Fig. 1) was performed by the gynecologic oncologist. There was active bleeding from excision site, which was sutured with 2/0 vicryl and hemostasis achieved. Tocolysis with Indomethacin 25 mg 8 hourly was started one day before the surgery, and continued for three days postoperative period with continued maternal and fetal monitoring. The histopathology report (examined by two experienced pathologists) showed moderately differentiated invasive squamous cell carcinoma of cervix (SCC) with lymphovascular space invasion (LVSI) (Fig. 2a and b). Base of the

resection margin showed presence of tumor. Magnetic Resonance Imaging (MRI) scan revealed broadened cervix, normal bilateral parametria with no obvious pelvic lymph nodes enlarged.

After breaking the news and counseling of the patient and her family members about SCC FIGO IB3, she was jointly managed by maternal fetal medicine (MFM) specialist and gynecologic oncologist. She was followed up every two weeks by MFM: monitoring for abnormal vaginal bleeding and discharges, fetal growth scan and regular supplements. Considering the locally available neonatal facilities, a consensus was reached to take the pregnancy up to 37⁺ weeks, and terminate by elective classical cesarean section with cesarean-radical hysterectomy. She had an uneventful antenatal period, and was admitted to the maternity ward at 37⁺² weeks of pregnancy for definitive obstetrical and oncological treatment.

After taking a written informed consent, elective classical cesarean section (Fig. 3) followed by cesarean-radical hysterectomy (Fig. 4) with bilateral salpingectomy with bilateral pelvic lymph nodes dissection with bilateral ovarian transposition to the para-colic gutters was performed with midline vertical incision under general anesthesia. A live male baby weighing 2.7 kg was delivered. Intraoperative assessment showed normal bilateral fallopian tubes and ovaries, free bilateral parametria and no enlarged bilateral pelvic and para-aortic lymph nodes. There was approximately 1000 ml blood loss. However, tissue plane identification and dissection were easier as compared to open-radical hysterectomy in the surgeon's experience. The resected specimen is shown in Fig. 4. The final histopathology (examined by two pathologists) revealed focal high grade squamous intraepithelial lesion (cervical intraepithelial neoplasia III) with glandular involvement. There was no residual malignancy seen. The vaginal margin, parametrium and lymph nodes were negative for malignancy.

In the postoperative period, she had uneventful recovery with minor surgical site infection. Urethral catheter was removed on postoperative day 10. Ultrasound scan after catheter removal showed maximum cystometric capacity (MCC) of 400 ml and postvoid residual volume (PVR) of 60.4 ml. She didn't complain of any lower urinary tract symptoms. She was advised for timed urinary voiding.

After counseling, she is kept under surveillance with the plan of three-monthly review for first two years, followed by every six months in 3–5 years.

At three months follow up, both mother and child were in good health. She didn't have postmenopausal symptoms. The findings of speculum and recto-vaginal examination were normal.



Fig. 3 Classical cesarean section uterine scar in a 27-year-old woman at 37⁺² weeks pregnancy with cervical cancer, which was followed by cesarean-radical hysterectomy

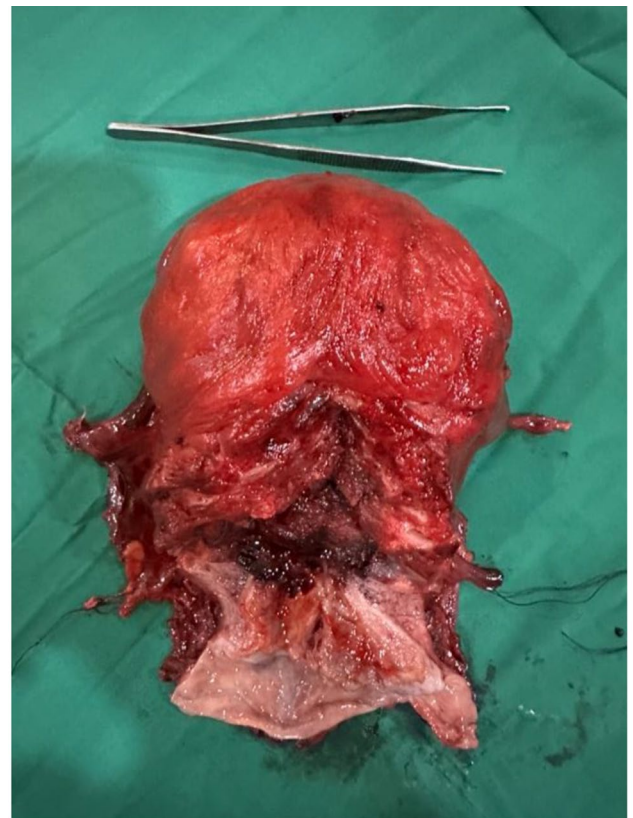


Fig. 4 Resected cesarean-radical hysterectomy specimen in a 27 year old pregnant woman with cervical cancer

Discussion and conclusion

Herein, we present a 27-year-old, primipara, whose cervical cancer was diagnosed at 28⁺⁵ weeks gestation, and treated with cesarean- radical hysterectomy (RH) with bilateral salpingectomy (BS) with bilateral pelvic lymph nodes dissection and bilateral ovarian transposition at 37⁺³ weeks gestation. To the best of authors' knowledge, this is the first such a case from Bhutan.

Cervical cancer in pregnancy is most commonly diagnosed gynecological malignancy during pregnancy with incidence of 0.1 to 12 per 10,000 pregnancies [2]. Diagnosis of cervical cancer during pregnancy or 6–12 months postpartum period is referred to as cervical cancer in pregnancy. In our case, she presented with fresh vaginal spotting at 27⁺ weeks pregnancy. The diagnosis was delayed, as the speculum examination of cervix was not performed. In a study, 7.6% of cervical cancer in pregnancy is diagnosed by physical examination and 6.7% by abnormal cervical cancer screening test [5]. In Bhutan, the national cervical cancer screening is recommended for women between 30 and 65 years, using HPV-DNA test every five years. Pregnant women don't receive routine cervical cancer screening services. In Japan, the implementation rate of cervical cytology during pregnancy was 86.8% [9].

Management of cervical cancer in pregnancy is complex, and involvement of multidisciplinary team would improve the quality of care [10]. Several issues are important when treating pregnant woman with cervical cancer: type of histology, status of lymph nodes, gestational age, and woman's wishes concerning continuation *versus* termination of pregnancy [4, 10]. The primary aims of the recommended treatment are the oncological safety of mother, and fetal survival without additional morbidity [10].

In our patient, we took all the possible factors into consideration while deciding to terminate the pregnancy at 37⁺ weeks. Firstly, the diagnosis of cervical cancer was doubly confirmed by two independent senior pathologists. Gynecologic oncologist, maternal fetal medicine specialist, neonatologist and patient were involved in finalizing the treatment decision. In Bhutan, we don't have medical and radiation oncologist, who otherwise could have provided significant professional input. In order to optimize the neonatal outcome, considering that this would be her only child, we decided to terminate pregnancy at 37⁺ weeks of gestation. The time from diagnosis to surgery was 61 days. In a retrospective study in China, the mean time from diagnosis to surgery in patients who continued pregnancy group was statistically significantly greater than the pregnancy termination group (52.7 vs. 16.3 days, $p < 0.01$), with no survival differences between the two groups (100% vs. 90.91%, $p = 0.54$). The authors concluded that continuation of pregnancy

with cervical cancer may not affect maternal oncologic outcome nor increase obstetric or surgical complications [11].

European Society of Gynecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology (ESGO/ESTRO/ESP) 2023 guidelines on cervical cancer recommends treatment of cervical cancer in pregnancy in a gynecological oncology center associated with the highest-level perinatal care [10]. Cesarean section is recommended for pregnancy with cervical cancer, as spontaneous vaginal delivery appears to have negative prognostic impact. Definitive cancer specific treatment should be performed at the time of cesarean section [10]. Vaginal delivery has risk of vaginal laceration, massive hemorrhage and metastasis of cancer [1]. Classical uterine incision can reduce bleeding and avoid damaging the blood vessels of tumours. Placenta should be sent for histopathological examination to look for possible metastasis [1, 12].

In non- pregnant women with stage IB3 who have no future fertility desires, the National Comprehensive Cancer Network (NCCN) recommends radical hysterectomy with pelvic lymphadenectomy with or without para-aortic lymphadenectomy or pelvic external beam radiation therapy (EBRT) with concurrent platinum-containing chemotherapy with brachytherapy [13]. Ovarian preservation needs to be discussed in women of reproductive age with squamous cell carcinoma. It can be considered in adenocarcinoma associated with HPV, and it is not recommended in HPV-independent adenocarcinoma of cervix. Regarding the ovarian transposition, it has to be discussed preoperatively and individualized according to the risk. If ovaries are preserved, opportunistic salpingectomy is recommended [10].

Management of stage IB3 cervical cancer in pregnancy is controversial, for which either neoadjuvant chemotherapy (NACT) or termination of pregnancy was recommended by International Network on Cancer, Infertility and Pregnancy (INCIP) if cancer is diagnosed before 22 weeks of gestation [14]. In locally-advanced cancer (>4 cm) diagnosed before 18 weeks of gestation, French guidelines proposes termination of pregnancy, whereas the European consensus meeting guidelines propose NACT as first line therapy [15]. The use of NACT (Paclitaxel and cisplatin) in pregnancy was found safe [11], and NACT (carboplatin and paclitaxel) plus radical hysterectomy in pregnancy with stage IB3 cervical cancer was found safe [12].

In our case, despite tumour size of 6*6 cm, NACT was not considered as the tumour growth was polypoidal with a narrow pedicle (about 2 cm width) arising from 6 to 9 o'clock position of cervix. In addition, during the antenatal surveillance, there was no macroscopically visible cervical growth, despite the histology report of positive

tumor at the resection margin. Considering her young age and in case of possible adjuvant radiation therapy requirement, bilateral ovaries were preserved and transpositioned to the para-colic gutters. However, placenta was not sent for histology examination, as the surgeon was not aware of the significance of histological assessment to look for possible metastasis in the placenta.

A study in US found that the cesarean-radical hysterectomy compared with open-radical hysterectomy was associated with an increased risk of hemorrhage (27.1% vs. 13.8%), ileus/small bowel obstruction (15.8% vs. 8.8%), and pyelonephritis (1.9% vs. 0.1%), but a decreased risk of atelectasis (0% vs. 5.6%), wound complications (0% vs. 2.5%), and respiratory failure (0% vs. 2.4%; all, $P < 0.05$) [7]. In our case, we experienced slightly higher blood loss (1000 ml) compared with open-RH. However, identification of tissue planes was better than in open-RH, and we could resect parametrial tissues and vaginal length better. In the postoperative period, other than minor surgical site infection, patient had an uneventful recovery.

In conclusion, this is the first case report of cervical cancer in pregnancy from Bhutan. She was successfully managed with optimal oncological and neonatal outcome with continuation of pregnancy to term. In a pregnant woman presenting with abnormal vaginal bleeding, a simple vaginal speculum examination may diagnose cervical cancer on time.

Abbreviations

CIN	Cervical Intra-epithelial Neoplasia
DNA	Deoxy ribose Nucleic Acid
ESGO	European Society of Gynecological Oncology
ESP	European Society of Pathology
ESTRO	European Society for Radiotherapy and Oncology
FIGO	The International Federation of Gynecology and Obstetrics
HPV	Human Papilloma Virus
INCP	International Network on Cancer, Infertility and Pregnancy
MCC	Maximum Cystometric Capacity
MFM	Maternal Fetal Medicine
NACT	Neo-Adjuvant Chemotherapy
NCCN	National Comprehensive Cancer Network
PVR	Post-void residual volume
RH	Radical Hysterectomy
SCARE	Surgical CAse REport

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Author contributions

ND: Conceptualised and wrote the manuscript, performed caesarean-radical hysterectomy, analysed and interpreted the data. RR: Involved in antenatal care and decision making, conceptualised manuscript. NC: Performed pathological evaluation and final interpretation. ST: Conceptualised manuscript and data interpretation. SD: Involved in patient care, Data collection and interpretation. All the authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Our institution does not require ethical approval for reporting de-identified individual case report.

Consent for publication

Written informed consent for publication was obtained from the patient.

Competing interests

The authors declare no competing interests.

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