

Case Report**Treatment Approach for a Rare Case of Cervical Cancer in Pregnancy*****Pendekatan Terapi pada Kanker Serviks dalam Kehamilan*****Yuannita I. Putri, Gumilang Wiranegara***Badan Pengusahaan Batam Hospital
Batam***Abstract**

Objective: To add a new overview of cervical cancer in pregnancy and to review several treatment approaches using available guidelines.

Methods: Case report.

Case: A 29 years old woman, gravida 3 para 2 in 10 weeks of pregnancy, was presented with vaginal bleeding and bloody vaginal discharge. Ultrasound examination showed a 10 weeks single live intrauterine fetus and a mass on the cervix. The histopathological report revealed a poorly differentiated cervical adenocarcinoma without invasion of lymphovascular space. Patient was diagnosed with cervical carcinoma FIGO stage IB3 in 10 weeks of pregnancy. The patient opted to unpreserved the pregnancy. Radical hysterectomy with fetus in situ and bilateral pelvic lymphadenectomy was performed. Patient was referred to undergo adjuvant radiation therapy.

Conclusion: Cervical cancer in pregnancy is a rare and special condition that requires individual planning for the diagnostic and treatment approaches.

Keywords: cervical cancer, cervical cancer in pregnancy, fetus in situ hysterectomy, pregnancy, radical hysterectomy.

Abstrak

Tujuan: Untuk menambah gambaran kasus mengenai kanker serviks dalam kehamilan serta membahas pendekatan terapi menggunakan pedoman – pedoman yang ada.

Metode: Laporan kasus.

Kasus: Seorang perempuan berusia 29 tahun dengan G3P2 usia kehamilan 10 minggu datang dengan keluhan perdarahan pervaginam dan keputihan bercampur darah. Hasil dari USG menunjukkan adanya janin berusia 10 minggu serta massa pada serviks. Hasil pemeriksaan histopatologi menunjukkan adanya adenokarsinoma serviks berdiferensiasi buruk tanpa invasi limfovaskuler. Pasien didiagnosis dengan kanker serviks stadium FIGO IB3 dalam kehamilan 10 minggu. Pasien setuju untuk dilakukan terminasi kehamilan. Pada pasien kemudian dilakukan laparotomi histerektomi radikal dengan fetus in situ serta limfadenektomi pelvik bilateral. Pasien kemudian dirujuk untuk dilakukan terapi ajuvan dengan radiasi.

Kesimpulan: Kanker serviks pada kehamilan merupakan suatu kondisi khusus sehingga perencanaan diagnostik dan manajemen terapi membutuhkan perencanaan secara individual di setiap kasusnya.

Kata kunci: Kanker, kanker serviks, kanker serviks dalam kehamilan, , histerektomi radikal, histerektomi dengan fetus in situ.

Correspondence author. Yuannita I. Putri. Badan Pengusahaan Batam Hospital. Batam
Email: yuannitaip@gmail.com

Received: February, 2021 Accepted: March, 2022 Published: April, 2022

INTRODUCTION

Cervical cancers are the second commonest cancer in Indonesian women. The incidence rate of cervical cancer in Indonesia is increased 17% between 1990 and 2017. The mortality rate is also increased, which 3,3 per 100.000 in 1990 and 3,7 per 100.000 in 2017.¹ The incidence rate of cervical cancer in pregnancy is extremely low. Of all women who were diagnosed with cervical cancer, 1 – 3% were diagnosed when

pregnant or postpartum.² Cervical cancer is the most common gynecological cancer founded in pregnancy with incidence rate of 1,5 – 12 per 100.000 pregnancies.³

Studies regarding cervical cancer in pregnancy are still limited. Many treatment approaches of cervical cancer in pregnancy still aroused many controversies. This paper aims to add a new overview of cervical cancer in pregnancy and to review several treatment approaches using available guidelines.

CASE

A 29-year-old woman with gravida 3 para 2 was presented with vaginal bleeding. The bleeding had been occurred for 3 months even before the pregnancy. The patient has been experiencing irregular menstrual bleeding for one year. Patient also complained of having bloody vaginal discharge frequently. The patient had menarche at 14 years old. She was married at the age of 18. Her obstetric history shows that the patient had two children, who had been delivered by spontaneous vaginal delivery. She was using IUD as a contraceptive method and had been removed one year ago. Ultrasound examination showed a 10 weeks single live intrauterine fetus and a mass on the cervix. The measurement of the mass is 7 x 6 x 6 cm. The

patient underwent cervical biopsy afterward. The histopathological report revealed a poorly differentiated cervical adenocarcinoma without invasion of lymphovascular space. Patient was diagnosed with cervical carcinoma FIGO stage IB3 in 10 weeks of pregnancy.

After the patient was educated and counseled regarding her condition, she opted to end the pregnancy. Radical hysterectomy with fetus in situ and bilateral pelvic lymphadenectomy was performed. Post-surgical histopathological report revealed cervical adenocarcinoma with an invasion of lymphovascular space, remaining of the implantation in the endometrium, absen of pelvic lymph nodes metastasis, no parametrium invasion, and negative surgical margin. Patient was referred to undergo adjuvant radiation therapy.

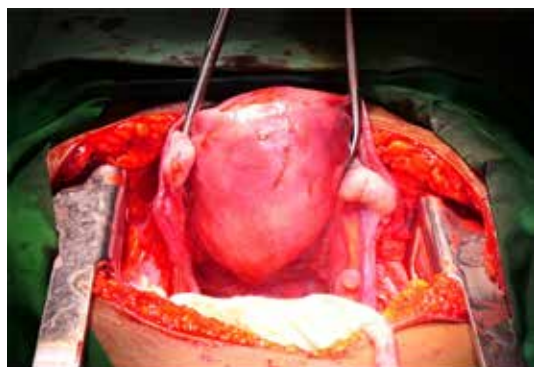


(a)



(b)

Figure 1. Ultrasound examination: (a) 10 weeks fetus with a cervical mass, (b) cervical mass with measurement 7x6x6 cm



(a)



(b)

Figure 2. Intraoperative: (a) Fetus in situ radical hysterectomy, (b) Absent of metastatic tumors macroscopically after radical hysterectomy

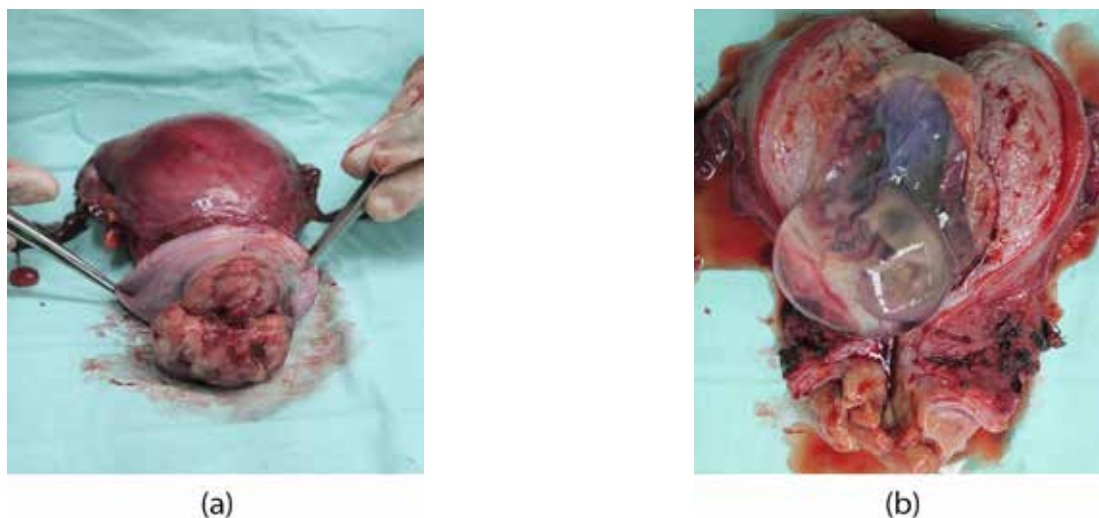


Figure 3. Radical hysterectomy specimen: (a) cervical mass, (b) fetus in situ

DISCUSSION

Many factors had to be considered when selecting the best treatment for cervical cancer in pregnancy. Stage of the disease, lymph nodes status, histological subtype, gestational age, obstetric complication, and patient's desire to continue or stop the pregnancy will affect the treatment options.⁴ Pregnancy can affect cervical cancer treatment and vice versa. However, the course of the disease and the disease prognosis are similar in pregnant and non-pregnant women.⁵

In this case report, the patient underwent a cervical biopsy to confirm the diagnosis. Cervical biopsy in pregnant women did not increase obstetric complications, miscarriages, and preterm labor. However, the sample collection must be done cautiously because the cervix during pregnancy is prone to bleeding. It is recommended that the depth of biopsy should less than 1 cm should not be too large so that the bleeding can be easily controlled.² Staging was determined using FIGO 2018 stage based on patient's histopathological result. Stage IB3 was the final diagnosis because clinically the tumor is limited on the cervix uteri with > 4 cm size and there is no sign of lymph node metastasis or distant metastasis.⁶

Treatment considerations of this patient were the gestational age (10 weeks of pregnancy), stage IB3, negative lymph nodes status, adenocarcinoma type of tumor, and patient's desire. A case in Portugal also reported the same treatment in 16 weeks pregnant woman with cervical carcinoma FIGO stage IB1 who

decided not to continue the pregnancy. Radical hysterectomy has been proved to be the best option for early-stage cervical cancer in patient who desired not to continue the pregnancy.⁷ Study from Maryland recommends immediate definitive treatment should be undergo in patient with endophytic, deeply invasive, poorly differentiated squamous cell tumor or adenocarcinoma. Radical hysterectomy with fetus in situ can be performed at gestational age below 20 weeks. In patient with undesired pregnancy with cancer diagnosed above 20 weeks, evacuation of the implantation in the uterus should be performed prior to radical hysterectomy.⁸ Indication of post-operative adjuvant radiotherapy has been determined by evaluating prognostic risk factors for recurrence.⁹ This patient has been met intermediate-risk group criteria because of the lymphovascular space invasion in the post operative histopathologic result. A study shows that adjuvant radiotherapy administration can decrease the risk of recurrence by 47%.⁹

Delayed treatment to wait for fetal maturity can be beneficial to the fetus but may affect the tumor progression.⁷ Study shows the 5 years disease specific survival for delayed treatment is 61%, whereas for the immediate action is 86%.¹⁰ Administration of NACT can help to control the tumor progression. NACT has been applied in a case of 21 weeks pregnant woman with cervical carcinoma FIGO stage IB1 in China, who wanted to continue the pregnancy. The patient had been delivered a live male baby via transabdominal cesarean section. Radical hysterectomy, bilateral salpingectomy, bilateral ovarian transposition, and pelvic lymphadenectomy

were also performed in this patient. The patient subsequently underwent 35 sessions of radiation therapy. In 3 years of follow up, there are no recurrency on the patient and the neonate has a good prognosis.¹¹ Another case involving NACT administration in cervical carcinoma stage IIB in desired pregnancy, presented a good outcome for the mother and the neonate.¹² Some studies showed that delayed treatment after delivery without NACT administration had been given a bad prognosis.^{7,13}

In 2014, International Institute of Gynecological Oncology (IGCS) dan European Society of Gynecological Oncology (ESGO) established fetal preservation program as a treatment approach for cervical cancer in pregnancy. This program focused on the administration of neoadjuvant chemotherapy (NACT) until the fetus is matured.² In 2018, Chinese Anti-Cancer Association (CACA) established a new guideline of cervical cancer in pregnancy treatment. The highlights of this guideline are patient with stage IA2 – IV within first 20 weeks of pregnancy, continuing the pregnancy is not recommended. Whereas treatment for second trimester of pregnancy still aroused controversies. Patient with stage IA – IIA who desired to continue the pregnancy, pregnancy can be continued with strict monitoring. Patient with stage IIB and above, continuing the pregnancy is not recommended. However, if the patient strongly desired the pregnancy, NACT can be applied as proposed by the European consensus.¹¹ The newest guideline was established in 2019 by International Network on Cancer, Infertility, and Pregnancy (INCIP) based on The Third International Consensus Meeting. In this guideline, stage of the disease and the gestational age are crucial points in treatment determination. It is recommended to use updated FIGO 2018 to stage the disease. Pelvic lymph node dissection is recommended for stage IA2, IB1, and IB2 below 22 weeks of pregnancy. If there is positive lymph node, termination of pregnancy is required. If the lymph node involvement is absent, simple trachelectomy or delayed treatment after delivery can be applied. For the same stages but with gestational age above 22 weeks, NACT or delayed treatment after delivery can be applied. For stage IB3, NACT can be applied or termination of pregnancy can be performed in gestational age below 22 weeks. For gestational age above 22 weeks, NACT or delayed treatment after delivery can be applied. Termination of pregnancy is recommended in

advanced stages (stage IIB and above), presence of lymph nodes metastasis, or if the patient desires to stop the pregnancy. In some operable cases (stage IA2 – IB2), radical hysterectomy with fetus in situ can be performed in first trimester and early second trimester. Whereas for stage IB3 and above, chemoradiation therapy should be done prior.¹⁴ In Indonesia, diagnostic and treatment approaches for cervical cancer in pregnancy have been using a guideline from Indonesian Society of Gynecologic Oncology. The treatment approach in this guideline is based on stage of the disease and gestational age. At 16 – 20 weeks of gestation, it is recommended to perform immediate surgery or chemoradiation. In second trimester of pregnancy and afterward, surgery and chemotherapy can be applied in certain cases to preserve the pregnancy. Above 20 weeks of pregnancy, delayed treatment can be opted in stage IA2 and IB1. When the fetus is viable, transabdominal cesarian section can be performed followed by radical hysterectomy. Adjuvant chemotherapy is recommended in locally advanced disease.¹⁵

CONCLUSIONS

Cervical cancer in pregnancy is a rare and special condition that requires individual planning for the diagnostic and treatment approaches. Patients' desire for pregnancy must be included in consideration of the treatment approach in addition to the stage, gestational age, lymph nodes status, and histologic types. Updated guidelines that can be a reference are guidelines from INCIP, IGCS, ESGO, CACA, and PNPk HOGI. For patients who don't desire to continue the pregnancy, radical hysterectomy with or without radiation therapy can be opt in early trimester. Currently, NACT administration for cervical cancer to preserve pregnancy has been applied in many cases. However, studies regarding the outcome of NACT administration are still limited, particularly in Indonesia. Further studies regarding NACT administration and outcomes in Indonesia should be developed to complement the current guideline.

REFERENCES

1. Wahidin M, Febrianti R, Susanty F. Burden Cervical Cancer in Indonesia: Findings from the Global Burden Disease Study 1990 - 2017. *Advances Health Sci Research*. 2020;22:213-6.
2. Beharee N, Shi Z, Wu D, Wang J. Diagnosis and Treatment of Cervical Cancer in Pregnant Women. *Cancer Med*. 2019;00(1-6).
3. Hunter M, Tewari K, Monk B. Cervical Neoplasia in Pregnancy. Part 2: Current Treatment of Invasive Disease. *Am J Obstet Gynecol*. 2008 ;199(1):10-8.
4. Han S, Gziri M, Calsteren KV, Amant F. Cervical Cancer in Pregnant Women: Treat, Wait, or Interrupt? Assessment of Current Clinical Guidelines, Innovations, and Controversies. *Ther Adv Med Oncol*. 2013 ;5(4):211-9.
5. Hopkins M, Morley G. The Prognosis and Management of Cervical Cancer Associated with Pregnancy. *Obstet Gynecol*. 1992;80:9-13.
6. Bhatla N, Berek JS, Fredes MC, Denny LA, Grenman S, Karunaratne K, et al. Revised FIGO Staging for Carcinoma of The Cervix Uteri. *Int J Gynecol Obstet*. 2019;145:129-35.
7. Ribeiro F, Correia L, Paula T, Santana I, Pinto L, Borrego J, et al. Cervical Cancer in Pregnancy: 3 Cases, 3 Different Approaches. *J Low Genit Tract Dis*. 2013;17(1):66-70.
8. Nguyen C, Montz F, Bristow R. Management of Stage I Cervical Cancer in Pregnancy. *Obstet Gynecol Surv*. 2000 ;55(10):633-43.
9. Takekuma M, Kasamatsu Y, Kado N, Kuji S, Tanaka A, Takahashi N, et al. The Issues regarding Postoperative Adjuvant Therapy and Prognostic Risk Factors for Patients with Stage I-II Cervical Cancer: A Review. *J Obstet Gynaecol Res*. 2017 ;43(4):617-26.
10. Ma J, Yu L, Xu F, Yi H, Wei W, Wu P, et al. Treatment and Clinical Outcomes of Cervical Cancer during Pregnancy. *Ann Transl Med*. 2019;7(11):241.
11. Han J, Hu X, He X, Wang J, Mueller M, Papadia A, et al. Cervical Cancer in Pregnancy: One Case Report and A Review of Current Treatment Recommendations. *Gynecol Pelvic Med*. 2019;2(10).
12. Palaia I, Pernice M, Graziano M, Bellati F, Panici P. Neoadjuvant Chemotherapy Plus Radical Surgery in Locally Advanced Cervical Cancer during Pregnancy: A Case Report. *Am J Obstet Gynecol*. 2007;197(4):5-6.
13. Elhassan E, Mirghani O, Mohamadani A, Ahmed B, Miskeen E. Cervical Carcinoma in Pregnancy: Case Report. *Gynecol Perinatol*. 2009;18(2):93-5.
14. Amant F, Berveiller P, Boere I, Cardonick E, Fruscio R, Fumagalli M, et al. Gynecologic Cancers in Pregnancy: Guidelines Based on A Third International Consensus Meeting. *Ann Oncol*. 2019 1;30(10):1601-12.
15. HOGI. Pedoman Nasional Pelayanan Kedokteran Kanker Ginekologi. 2018.