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Case Report

Double fatal consequences of distance metastasis in nasopharyngeal carcinoma after a completed chemoradiation in pregnancy: A case report

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Abstract

Distant metastasis in nasopharyngeal carcinoma (NPC) patients is one of the reasons for the decreased life expectancy with the most common metastasis spreads are to the bone, liver, and lung. Hepatoma is the most frequent liver malignancy and is one of the highest causes of cancer death worldwide and this can be as a result of NPC metastasis. The aim of this case report was to present a patient with hepatoma in pregnancy as a result of NPC metastasis. A 34-year-old pregnant female at 24–25 weeks of gestation presented with a chief complaint of heartburn and unbearable pain radiating to the back. Previous medical history reported that the patient had a liver enlargement. The patient was G4P2A1 with a single living intrauterine fetus and active fetal movements. The patient has a history of NPC and received a completed chemoradiation one month prior to hospital admission. Physical examination showed bilateral rales and palpable diffuse multiple nodule masses in the upper right abdominal quadrant. Laboratory examination revealed anemia, thrombocytopenia, negative hepatitis B surface antigen (HBsAg), and elevated liver markers. Abdominal ultrasonography results showed multiple diffuse nodules in the liver. The patient was diagnosed with a metastatic hepatoma based on the clinical and imaging findings. During hospitalization, the patient repeatedly experienced pleural effusion with suspicion metastases. A few days later, the fetal movements stopped and the ultrasonography indicated negative fetal heart rate. After experiencing respiratory distress for hours, the patient expired the day after. This case highlights that due to the potential adverse effects of chemotherapy and radiotherapy, the initiation of these therapies should be carefully decided to avoid adverse effects to mother and fetus.

Keywords: Nasopharyngeal carcinoma, metastasis, intrauterine fetal death, hepatoma, chemotherapy

Introduction

Nasopharyngeal carcinoma (NPC) is a squamous cell carcinoma arising from the nasopharyngeal epithelium, making it the most common malignancy in the nasopharynx. NPC is endemic in Asia and Africa and its incidence varies greatly by country [1]. The highest incidence was reported in southern China with 25 to 50/100,000 population, and the lowest was in Europe with 1/100,000 population [1]. This could be related to the role of genetics in susceptibility to the Epstein-Barr virus (EBV) [2,3]. Men are more predisposed to NPC than women [3].

The incidence of NPC in Indonesia reached 6.2/100,000, with nearly 13,000 new cases, but

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the data is expected underreported [4]. A study reported that NPC is the most common head and neck cancer in Indonesia (28.4%), and is endemic to Java Island [5]. The incidence of NPC in pregnant women is rare, less than 1/100,000 per year [6].

Distant metastasis in NPC patients is one of the reasons for the decreased life expectancy with the most common metastasis spreads are to the bone, liver, and lung [7]. Hepatoma is the most frequent liver malignancy and is one of the highest causes of cancer death worldwide [8]. This cancer can be as a result of NPC metastasis. The incidence of cancer together with pregnancy is a rare case and when it occurs it is a challenging situation; the risks and benefits of oncology therapies must be balanced for the mother and fetus benefits [6,9]. Oncological treatment is preferred over the termination of pregnancy. A 20-year cohort study showed that 1170 cancer patients presented with live births [10]. However, preterm labor is a major side effect of pregnancy and should be avoided [10,11]. The aim of this case report is to present fatal consequences (mother and fetus) of hepatoma as a result of distance metastasis of NPC during pregnancy.

Case

A 34-year-old pregnant female at 24–25 weeks of gestation presented to Department of Obstetrics and Gynecology at Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia on November 22, 2022 with a chief complaint of heartburn and pain radiating to the back. Previous medical history reported that the patient had liver enlargement; however, the patient declined any history of hepatitis. The patient also complained of a palpable mass on the upper right quadrant of the abdomen. The patient's obstetrics history revealed G4P2A1, with a single living intrauterine fetus and active fetal movements based on ultrasonography (USG) November 21, 2022 (**Figure 1**). There was no weight loss, spotting, and amniotic discharge. A history of gestational abortion was in the first pregnancy by curettage in 2014. Following that, the patient underwent cesarean delivery (C-section) twice. The patient has a history of NPC stage II based on clinical examination and anatomical pathology findings with non-keratinizing squamous cell carcinoma and received one complete series of chemoradiation in October 2022.

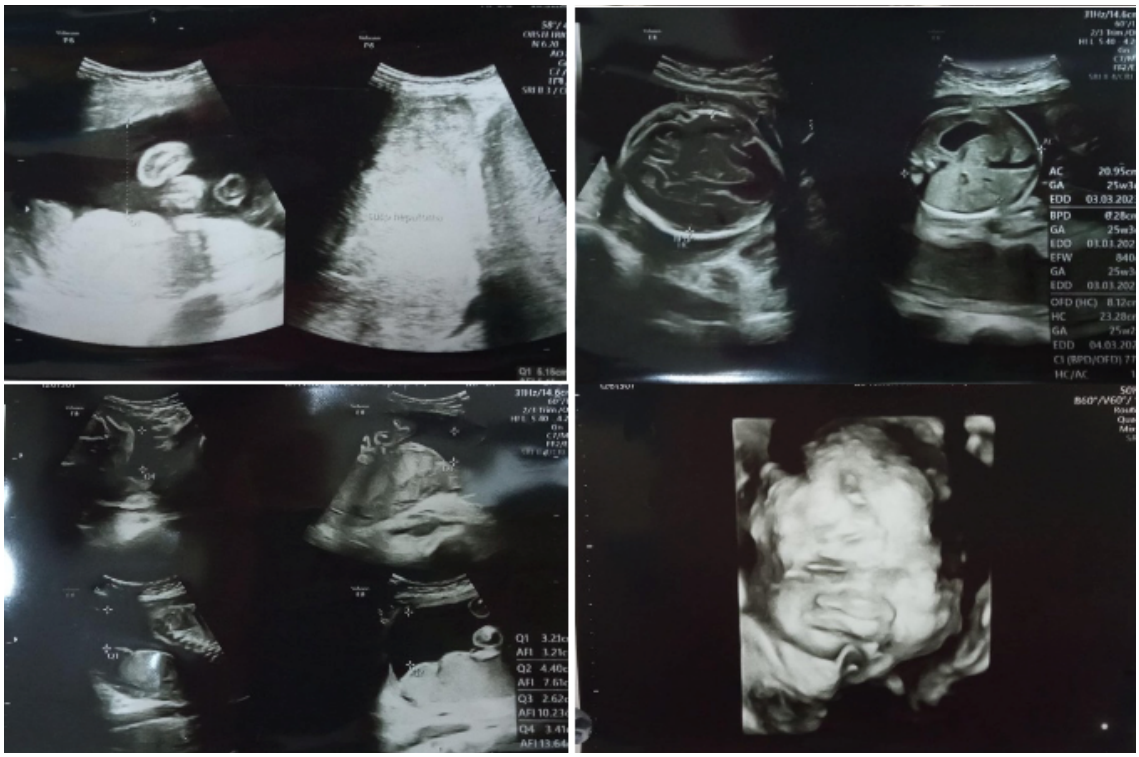

Figure 1. Fetal ultrasonography shows a single living intrauterine fetus with active movements (November 21, 2022).

Physical examination results showed bilateral rales and palpable diffuse multiple nodule masses in the upper right abdominal quadrant. Laboratory examination revealed anemia (10.3 mg/dL), thrombocytopenia (116x10^3/mm^3), negative hepatitis B surface antigen (HBsAg), and elevated serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT). The latest abdominal USG results (November 24, 2022) showed multiple diffuse nodules in the liver (**Figure 2**). The patient was diagnosed with a metastatic hepatoma process based on the clinical and imaging findings. The patient was then discharged on November 25, 2022 with administration of paracetamol 500 mg each 8 h, N acetyl cysteine 200 mg each 8 h, and curcuma, and patient was asked to return to poly control on December 01, 2022.

The patient returned to Dr. Zainoel Abidin Hospital on November 28, 2022 with intrauterine fetal death (IUFD) condition and respiratory failure. The USG examination was performed yielded negative fetal movements and negative fetal heart rate (**Figure 3**). On November 30, 2022 the patient died of respiratory failure due to pleural effusion.

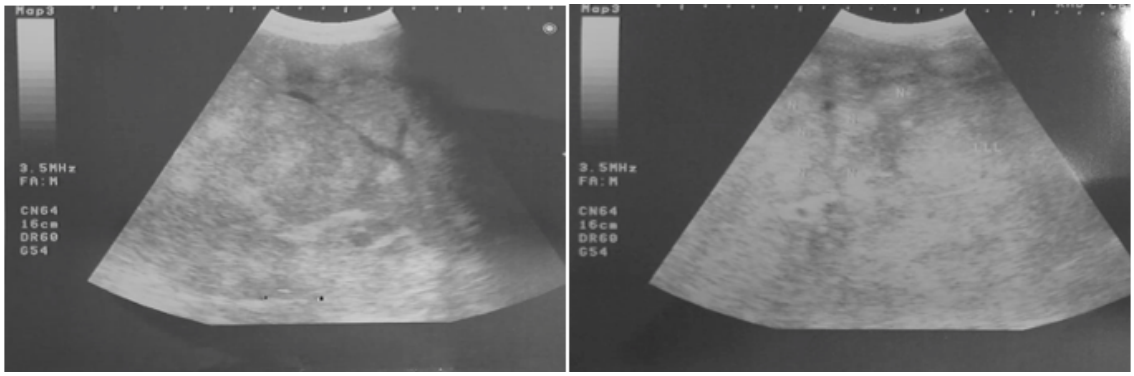

Figure 2. Abdominal ultrasonography detects the process of liver metastases (November 24, 2022).

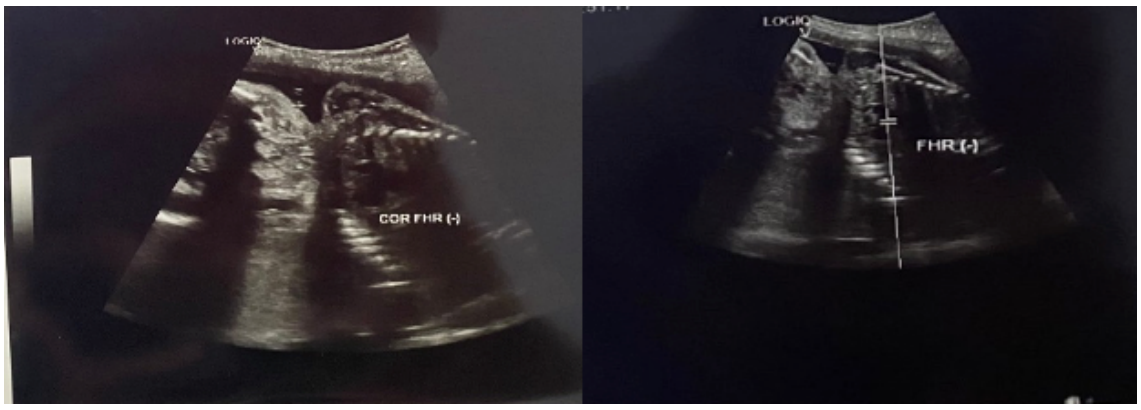

Figure 3. Fetal ultrasonography shows the absence of fetal heart rate (November 29, 2022).

Discussion

We reported a patient with a history of NPC and received chemoradiation who diagnosed with hepatoma due to NPC metastasis. Diagnosis using ionizing imaging during pregnancy should be minimized due to the teratogenic risks. The risk of stomatic carcinogenic effects from radiation depends on the gestational age at the time of the imaging examination. The cumulative fetal dose of radiation should not exceed 100 mGy. A radiologist and medical clinician should discuss radiation exposure to the fetus to assess each pregnant woman's estimated fetal dose levels [12]. Non-ionizing imaging procedures such as USG and magnetic resonance imaging (MRI) are the best techniques for assessing the staging of pregnant women. The effect on the fetus is unclear, but giving gadolinium (contrast MRI) is recommended considering the diagnostic benefits and fetal risks [12].

The patient in this present case report had a delayed diagnosis of hepatoma. A delay in therapy is associated with an increased risk of mortality. A prior study found that hepatoma

patients frequently have more than three-month delays in diagnosis and treatment; the reasons are often due to provider factors or decision-making, and patient factors [13]. The survival rate of patients with hepatoma without therapy is less than 12 months [14]. A delay in treatment of more than three months plays a role in tumor development and is associated with microvascular invasion [14]. A population-based study found that a mother's cancer diagnosis two years before pregnancy was associated with preterm birth, post-term birth, low birth weight, small gestational age, low Apgar score, and C-section [15]. Cancer can cause side effects on the fetus due to poor nutritional intake, impaired placental function associated with poor delivery of oxygen and nutrients to the fetus, and chronic inflammation [15].

The patient experienced anemia, which is a common complication of several types of cancer, including hepatoma. A study reported that long-term anemia associated with hepatic insufficiency and the stage of the hepatoma affected the patient's prognosis [16]. Hemoglobin level below 13 g/dL is associated with an increased risk of mortality and shortened survival in patients with hepatoma. Anemia affects the quality of life due to symptoms such as fatigue, shortness of breath, and loss of mental acuity. Anemia also causes hypoxia in the tissue environment. The oxygenation of the tumor is related to the level of blood flow, microcirculation, and hemoglobin concentration. Tumor hypoxia can lead to decreased local disease control and increase the potential for metastasis. Hypoxic tumor cells are chemoresistant and anemia also negatively affects the response to radiotherapy [16]. Infants born to anemic mothers have a twice greater risk of having low birth weight and preterm birth than mothers without anemia [17].

The patient has not received therapy for the treatment of hepatoma. Radiotherapy, followed by chemotherapy, is the best treatment option for advanced NPC and is one of the treatment options for hepatoma. Several factors must be considered before giving systemic therapy to pregnant women such as changes in the physiology of pregnancy, gestational age, passage of the placenta, and pharmacokinetics of the drug [12]. Physiological changes that occur due to exposure and the efficacy of systemic therapy affect the pharmacokinetics of the drug [12].

Chemotherapy drugs that enter transplacental can occur due to passive diffusion and are based on the molecular size of the drug, lipid solubility, ability to bind to proteins, and ionization. Chemotherapy drugs generally have a small molecular weight that is not bound and uncharged, so chemotherapy drugs can easily enter the human placenta [12,18,19]. Chemotherapy should be avoided in the first trimester of pregnancy to avoid organogenesis. After 12–14 weeks of gestation, administration of cytotoxic drugs can be given and is relatively safe. Standard chemotherapy regimens and doses are based on the mother's weight during pregnancy [12]. After 35 weeks of gestation, chemotherapy is avoided to allow time for bone healing for the mother and fetus from the last cycle of chemotherapy until delivery. Postpartum chemotherapy should be planned if indicated [12].

Cytotoxic drugs should be given after the period of organogenesis because the rate of congenital malformations in this period is 10–20%. Chemotherapy can cross the blood-placental barrier and cause fetal intrauterine growth restriction (IUGR). Other things that affect fetal growth are underlying disease of the mother, cytotoxic treatment, cachexia, psychological stress related to cancer, and malnutrition. Because of the frequent morbidity of preterm birth, iatrogenic preterm births are avoided whenever possible [12].

Chemotherapy during embryogenesis is associated with increased spontaneous abortion and major congenital disabilities, stillbirth, fetal IUGR, preterm birth, and maternal and fetal myelosuppression [20]. Complications to the fetus that can arise from chemotherapy during pregnancy are malformations, organ toxicity, death, and developmental delays to survive [20]. Complications in the mother's death due to delay in therapy can occur 1–3% however chemotherapy given early in pregnancy can increase fetal malformations, and low birth weight babies [20].

Radiation therapy should be avoided during pregnancy because of the high radiation dose to the fetus and serious complications or fetal death. Radiotherapy for non-pelvic cancer is limited to the first trimester when the uterus is still far from the radiation area. The total dose of an irradiated fetus is obtained from internal scattering, radiation leakage, and external scattering [12,21]. Because the effects of irradiation on the fetus vary with gestational age and radiation dose, careful consideration must be made of the patient's interests [12,21].

Continuing or termination of pregnancy did not show a reduction in maternal mortality. Upon this, early termination does not need to be done routinely because a delay in therapy in the second trimester does not show any change in outcome [20]. Another study reported women with terminated pregnancy had a poorer prognosis than those who extended their pregnancy [22]. Additionally, it is suggested that early delivery by C-section or induction is preferable to assist in initiating therapy [15]. However, this may result in low birth weight or iatrogenic preterm delivery [15].

In our case, the fetal death occurred before the death of the mother. Cancer diagnosis in the mother during pregnancy is associated with an increased risk of stillbirth in a small for gestational age (SGA) fetus and stillbirth is more common in mothers who have received cancer therapy [23]. However, cancer therapy is not the primary cause of stillbirth in women with cancer. Fetal IUGR and stillbirth can be caused by cancer. Leukemia and solid tumors (such as hepatomas) cause the supply of oxygen and nutrients to the fetus to be disrupted and the local inflammatory environment also impairs fetal growth and viability [23]. Psychological stress also contributes to the incidence of stillbirth and SGA during gestation [23].

Conclusion

Pregnant women diagnosed with cancer are associated with preterm birth, post-term birth, low birth weight, small gestational age, low Apgar score, C-section, and stillbirth. Chemotherapy and radiotherapy are treatment for NPC patients. However, during the pregnancy, radiation exposures to the mother and fetus should be carefully estimated to avoid adverse effects and further complications.

Ethics approval

The patient's family gave written consent for publication as a case report.

Competing interests

The authors declare that there is no conflict of interest.

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Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

How to cite

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References

1. Chang ET, Adami H-O. The enigmatic epidemiology of nasopharyngeal carcinoma. Cancer Epidemiol Biomark Prev 2006;15(10):1765-1777.
2. Du T, Xiao J, Qiu Z, *et al.* The effectiveness of intensity-modulated radiation therapy versus 2D-RT for the treatment of nasopharyngeal carcinoma: A systematic review and meta-analysis. PLoS One 2019;14(7):e0219611.
3. Shah AB, Nagalli S. Nasopharyngeal carcinoma. StatPearls. 2022.
4. Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.01.07/MENKES/684/2019 Tentang Pedoman Nasional Pelayanan Kedokteran Tatalaksana Kanker Nasofaring. Jakarta. 2019.

5. Adham M, Kurniawan AN, Muhtadi AI, *et al*. Nasopharyngeal carcinoma in Indonesia: epidemiology, incidence, signs, and symptoms at presentation. Chin J Cancer 2012;31(4):185-196.
6. Santoso S. Case report: Nasopharyngeal carcinoma in pregnancy. Int J Nasopharyngeal Carcinoma 2020;2(2):35-37.
7. Yang Y, Li X, Zhou P, *et al*. Survival effects of radiotherapy on patients newly diagnosed with distant metastatic nasopharyngeal carcinoma in non-high-incidence areas. Cancer Manag Res 2021;13:8169-8178.
8. Balogh J, Victor D, Asham EH, *et al*. Hepatocellular carcinoma: A review. J Hepatocell Carcinoma 2016;3:41-53.
9. Lambertini M. Cancer and pregnancy: A comprehensive review. Cancers 2021;13(12):3048.
10. de Haan J, Verheecke M, Van Calsteren K, *et al*. Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: A 20-year international cohort study of 1170 patients. Lancet Oncol 2018;19(3):337–346.
11. Maggen C, Wolters VERA, Cardonick E, *et al*. Pregnancy and cancer: The INCIP project. Curr Oncol Rep 2020;22(2):17.
12. Wolters V, Heimovaara J, Maggen C, *et al*. Management of pregnancy in women with cancer. Int J Gynecol Cancer 2021;31(3):314-322.
13. Rao A, Rich NE, Marrero JA, *et al*. Diagnostic and therapeutic delays in patients with hepatocellular carcinoma. J Natl Compr Cancer Netw 2021;19(9):1063-1071.
14. Liao Y-Y, Ou J, Luo C-P, *et al*. Does delayed treatment affect the survival of patients with hepatocellular carcinoma? Transl Cancer Res 2018;7(3):E14-E16.
15. Momen NC, Arendt LH, Ernst A, *et al*. Pregnancy-associated cancers and birth outcomes in children: A Danish and Swedish population-based register study. BMJ Open 2018;8(12):e022946.
16. Finkelmeier F, Bettinger D, Köberle V, *et al*. Single measurement of hemoglobin predicts outcome of HCC patients. Med Oncol 2014;31(1):806.
17. Aringazina R, Kurmanalina G, Bazargaliyev Y, *et al*. Impact of anemia in pregnant women on the neonatal conditions. Open Access Maced J Med Sci 2021;9(B):1185-1188.
18. Van Calsteren K, Verbesselt R, Beijnen J, *et al*. Transplacental transfer of anthracyclines, vinblastine, and 4-hydroxy-cyclophosphamide in a baboon model. Gynecol Oncol 2010;119(3):594-600.
19. Calsteren K V, Verbesselt R, Delieger R. Transplacental transfer of paclitaxel, docetaxel, carboplatin, and trastuzumab in a baboon model. Int J Gynecol Cancer 2010;20(9):1456-1464.
20. Yp Z, J D, Xw Z, *et al*. Maternal and neonatal outcomes of cancer during pregnancy: A multi-center observational study. J Cancer 2019;10(23):5727-5734.
21. Kal HB, Struikmans H. Radiotherapy during pregnancy: fact and fiction. Lancet Oncol 2005;6(5):328-333.
22. Abdel-Hady E-S, Hemida RA-H, Gamal A, *et al*. Cancer during pregnancy: perinatal outcome after in utero exposure to chemotherapy. Arch Gynecol Obstet 2012;286(2):283-286.
23. Lu D, Ludvigsson JF, Smedby KE, *et al*. Maternal cancer during pregnancy and risks of stillbirth and infant mortality. J Clin Oncol 2017;35(14):1522-1529.