Case Report

Cervical Adenocarcinoma in Pregnancy with a Concomitant Papillary Adenocarcinoma of the Thyroid Gland: A Case Report

Nicole Bolla, Katharina Putora, Livia Noemi Kolb and René Hornung*

Department of Obstetrics and Gynecology, Cantonal Hospital, St. Gallen, Switzerland

Abstract

Introduction: Cervical cancer in pregnancy is a rare disease, with an incidence of 0.01-0.1%, of which most are squamous epithelial cancers. We here present the first case of a uterine cervical adenocarcinoma during pregnancy with a concomitant papillary adenocarcinoma of the thyroid gland.

Materials and Methods: Data were extracted from the patient’s records. Literature review was performed using the databases PubMed, Web of science and Embase.

Case Report: A 36-year-old Gravida IV, Para III was admitted to the Cantonal Hospital St. Gallen, Switzerland with an invasive adenocarcinoma of the uterine cervix cT1B2 cNx Mx G1 ER neg PR neg Ki67 80% at 31 weeks of gestation. She was treated with 2 cycles of neoadjuvant chemotherapy (carboplatin and paclitaxel). Following caesarean section at 36 2/7 weeks of gestation, treatment was switched to chemoradiation therapy. The patient delivered a healthy girl. A concomitant papillary thyroid cancer pT1a, pN1a (1/6) was successfully treated by surgery. The patient is free of recurrence and metastasis at 4.5 years of follow-up for either of the tumors.

Conclusion: Management of cervical cancers in pregnancy has to be individualized based on factors like gestational age, stage and histology of the cancer, and the wish for pregnancy continuation or termination. Neoadjuvant chemotherapy seems to be a reasonable option to postpone radical surgery or chemoradiotherapy to prevent preterm delivery. To the best of our knowledge, this is the first report of a cervical adenocarcinoma in pregnancy with a concomitant papillary thyroid cancer.

*Correspondence to: Professor, Dr. René Hornung, M.D., Head of Department of Obstetrics and Gynaecology, Cantonal Hospital, Kantonsspital, Rorschacherstrasse 95, 9007 St.Gallen, Switzerland; Tel: 0041714941861; E-mail: rene.hornung@kssg.ch

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Material and Methods

The patient signed a written informed consent allowing the use of anonymized data for scientific publication. Data were extracted from the patient’s medical records. Literature review was performed using the databases PubMed, Web of science and Embase.

Case Report

The 36-year-old gravida IV, para III has a history without relevant events. One of her children is suffering from a Prader-Willi-Syndrome. The patient underwent regular gynaecologic checkups with no pathologic findings, the last of which was performed at the age of 34. The current pregnancy had regular obstetrical controls without pathologic findings. The patient was admitted to the obstetrical clinic of a cantonal hospital St.Gallen, Switzerland, in her 30th gestational week for an evaluation of the cervix with a suspected preterm ripening and consecutive prolapse of the amniotic membrane associated with recurrent vaginal bleedings. Clinical examination and a transvaginal sonography revealed a cervical length of 50mm and no risk of preterm delivery. However, a Pap smear showed a HSIL (high grade squamous intraepithelial lesion, Pap IV). A colposcopy-guided snip biopsy revealed an in part papillary structured, well differentiated adenocarcinoma of the endocervical type on all of the three examined locations staging the tumor into FIGO IB1. The tumor tissue did not express neither estrogen nor progesterone receptors, had few polymorphisms of the nuclei, was positive for p16 and had MIB-1 of 80% of the tumor nuclei. The MRI showed a cervical mass with an extent of 57 x 52 x 52 millimeters at the dorsolateral cervix on the left side, adjacent to the rectum but without infiltration of either the rectum or the parametria and with no enlarged lymph nodes or metastases, upgrading the tumor to stage IB2.

The fetal lung ripening was induced using 12mg betamethasone per day for two days. The case was discussed at our interdisciplinary tumor-board. Two cycles of neoadjuvant chemotherapy using carboplatin (300mg intravenous on day one, five and fifteen) combined with paclitaxel (75mg/m², 150mg intravenous on day one, eight and fifteen) were administered. At 36+2 gestational weeks a cesarean section was performed in spinal anaesthesia with a midline laparotomy and a midline longitudinal uterotomy (allowing axial traction on the uterus in case immediate radical hysterectomy would be necessary). Both parametria were free of tumor and no substantial mass of the uterine cervix was palpated. At the anterior cervical lip, a villous formation with a diameter of about 3cm was palpable and visible, suggesting residual tumor. The placenta was free of tumor. A healthy female neonate was delivered (APGAR 8/8/9, 2735g, 46cm). The late preterm baby suffered from an infant respiratory distress syndrome requiring initial continuous positive airway pressure ventilation and later a flow oxygenation for 2 days supported by oral administration of caffeine citrate to treat a bradycardia-apnea-syndrome. Because of poor weight gain due to insufficient breast feeding, a nasal stomach tube was installed for additional feeding. A neonatal hyperbilirubinemia was treated by phototherapy. In addition, perianal dermatitis was treated using a zinc ointment. The mother was discharged from the hospital 5 days following cesarean section and ablationation. A second MRI revealed a regression of the tumor size to 3.8 x 4.0cm and a PET scan confirmed an intensively focal FDG enrichment in the cervical tumor as well as a focal accumulation in a left thyroid lobe, with slight FDG-avid lymph nodes in the region of the jaw angle.

Following a second discussion at the tumor-board a percutaneous radiotherapy of the primary tumor as well as the lymphatic basin was administered to a total dose of 52.6Gy in fractions of 1.8Gy/d with concomitant administration of 6 cycles of weekly cisplatin chemotherapy (40mg/m² body surface area). At time of installation of the vaginal brachytherapy, histology still confirmed the presence of both, in situ and infiltrative adenocarcinoma of the cervical tissue. The radiation therapy was completed by an intracervical high dose brachytherapy with an additional dose of 5 x 5 = 25Gy.

The TSH value of 2.33 was within normal rage (0.25 - 4ml U/l). Thyroid sonography revealed a hypoechoogenic nodule of 13 x 8 x 12 millimeters in diameter in the left thyroid lobe without well-defined margins including micro calcifications. No suspect lymph nodes were seen. However, the margin of the tumor against the sternothyroid muscle was not well defined. Two ultrasound-guided fine needle aspirations revealed cells of a papillary thyroid carcinoma Bethesda classification VI and British classification Thy5. Therefore, a hemithyroidectomy of the left side together with cervico-central lymphadenectomy with partial resection of the sternothyroid muscle was performed. Histology revealed a papillary thyroid carcinoma with a diameter of 9mm. No tumor invasion or penetration through the organ capsule were seen with clear surgical margins. A Thyroid carcinoma metastasis with a diameter of 1.5 mm was found in one out of six lymph nodes (lymph node level 6/C1b) staging the tumor to pT1a, pN1a (1/6). A postoperative laryngoscopy demonstrated a normal larynx without signs of a recurrent nerve dysfunction. No adjuvant treatment was needed.

The patient undergoes routine follow-up consultations in both, the gynaecologic oncology as well as the endocrinology department and is free of recurrence 4.3 years following cancer treatment.

Discussion

Cervical cancer is among the most common cancers in pregnant women, however, with 4 per 100,000 pregnancies its incidence is rather low [4]. In addition, adenocarcinoma of the uterine cervix during pregnancy is even rarer [5]. Thyroid cancers in pregnancy are rare. The prevalence is 0.3 to 4 per 100,000 pregnancies [6, 7]. To the best of our knowledge, this is the first report of a cervical adenocarcinoma with a concomitant thyroid carcinoma during pregnancy. Management of cervical cancer during pregnancy is challenging because of the dilemma between appropriate oncologic therapies of the mother on the one hand and fetal survival without adverse effects due to potentially teratogenic treatments on the other hand. There is no gold standard for the management of these patients due to the lack of randomized controlled trials stratifying both, the gestational age and the tumor biology.

Surgery is the mainstay of treatment in early stage cervical cancers. However, radical surgery of cervical cancer during pregnancy cannot be performed safely for both, mother and child. Radiotherapy of cervical cancers cannot be applied during pregnancy due to adverse effects to the unborn child. The adverse effects include fetal death, mental retardation, microcephaly, iris defects, cataracts, skeletal anomalies and microphthalmia [8]. However, radiotherapy is a treatment option...
following termination of pregnancy by either abortion or delivery. Effects of chemotherapy during pregnancy on a child are still controversial [5, 9]. Chemotherapy during pregnancy may be associated with teratogenic effects on the fetus and the risk of miscarriage. Teratogenicity of a drug in pregnancy depends on the type of chemotherapy, its applied dose, the placental permeability of the drug, the time of fetal exposure to the drug as well as the gestational age [2]. Chemotherapy should not be applied during the first trimester. Most authors however believe that the risk of chemotherapy-induced congenital malformation seems not to be increased in second or third trimester pregnancies (i.e. later than 14 weeks of gestation) compared to those without exposure to chemotherapeutic agents [8]. However, preterm born children that were exposed to chemotherapy reveal more neurodevelopment problems, low birth weight, intrauterine growth retardation and prematurity than those born at term [2].

Based on weighing up preterm delivery against state of the art treatment of the FIGO 1B2 cervical adenocarcinoma we decided for a stepwise procedure. Starting at 30 weeks of pregnancy, we applied two cycles of chemotherapy (carboplatin and paclitaxel), followed by cesarean section and a standard radio-chemotherapy. The postpartum staging found a pT1a pN1a (1/6) papillary thyroid carcinoma that was treated by surgery. After almost five years of follow-up, the patient is free of recurrence of either of the cancers and the baby develops nicely. This suggests that the chosen treatment steps were reasonable for the present case.

Highlights

- This is the first report of cervical combined with thyroid cancer in pregnancy.
- Chemotherapy followed by surgery of cancer is reasonable to prolong pregnancy.
- The treatment of cancer in pregnancy focuses on the wellbeing of mother and child.

Author Contributions

Nicole Bolla is a fellow in gynaecologic oncologist, responsible for the oncological management of the patient and the acquisition of data for the manuscript. Katharina Putora is a fellow in foeto-maternal medicine and responsible for the obstetrical management of the patient the acquisition of data for the manuscript. Livia Noemi Kolb wrote a full review of the literature as her master thesis in human medicine and was in charge with the methodology of the case report. René Hornung is head of the department of Obstetrics and Gynaecology, main gynaecologic oncologist at the hospital and was involved in conceptualization and writing of the manuscript.

Disclosure

This case has not been published elsewhere before. None of the authors have financial interests in the present manuscript.

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