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Case report

Krukenberg tumor due to gastric cancer in pregnancy – Report of 2 cases

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Abstract

Krukenberg tumors (KTs) are 1-2% of all ovarian tumors, they are rare in pregnancy, and they have a poor prognosis since they are detected in advanced stages. We report 2 cases of KT in pregnancy. Bilateral giant solid adnexal masses were detected at the 25th gestational week in the 1st case and at the 14th gestational week in the 2nd case. Both of our patients had persistent nausea, vomiting, and abdominal pain. Salpingo-oophorectomy without gastrectomy was the procedure applied at the 25th and the 18th weeks in our cases, respectively. Chemotherapy was applied after the diagnosis of the KT. Preterm delivery, which is an expected complication in patients receiving chemotherapy during pregnancy, also occurred in our patients, and patients died 3 months and 5 months after the diagnosis, respectively. In conclusion, the adnexal region should be routinely checked during pregnancy. Cases with persistent gastrointestinal symptoms along with an adnexal mass should be evaluated with gastroscopy. The gestational week should be taken into account and a multidisciplinary approach should be applied.

Keywords

Krukenberg tumor, pregnancy, gastric cancer, adnexal mass, salpingo-oophorectomy, chemotherapy.

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Introduction

Cancer diagnosis during pregnancy is approximately 1 in 1,000 births. Most cases consist of cancers of the breast, thyroid, cervix, malignant melanoma, and Hodgkin lymphoma [1]. Krukenberg tumor (KT) is a metastatic tumor that develops secondarily in the ovaries, which is characterized by cells in the appearance of a signet ring, with the primary focus usually in the gastrointestinal tract. It usually manifests itself as ovarian metastasis of undiagnosed gastric cancer. The most common origin of KTs are gastrointestinal, 66.4% being gastric and 26.9% colorectal cancers [2]. While malignant adnexal masses constitute 3% of ovarian tumors in pregnancy, KT composes 1-2% of ovarian tumors [2]. Here, we present 2 cases of KT diagnosed during pregnancy.

Case 1

A 36-year-old, gravida 4, parity 2 woman applied to our center at the 25th week of gestation due to abdominal swelling and dyspnea that started 1 month prior. The patient had chronic hypertension and type 2 diabetes and was receiving alpha methyl dopa and insulin therapy. She reported an ongoing but worsening nausea and vomiting that began in the 6th week.

Her heart rate was 86 bpm, but oxygen saturation in room air was 90%. She reported abdominal pain, inability to lie down, loss of appetite, severe nausea and vomiting, and her abdomen was significantly distended. She also had difficulty in breathing. The levels of urea (20 mg/dL), and creatinine (0.52 mg/dL) were normal, but the albumin (2.1 g/dL), hemoglobin (9 g/dL), and platelet counts (82 × 10^4 µL) were abnormal. Serum cancer antigen 125 (CA-125) (1,051 U/mL), cancer antigen 19.9 (CA-19.9) (2,043 U/mL), carcinoembryonic antigen (CEA) (407 ng/mL) were markedly elevated. On ultrasound, the fetus was appropriate in size for 25 weeks and had no major fetal anomaly. However, a 165 x 135 mm right and a 170 x 165 mm left adnexal heterogeneous solid masses and diffuse free fluid in the abdomen were detected (**Fig. 1**). Bilateral pleural effusion and a 5 mm nodule in the posterobasal segment of the left lower lung lobe were observed in the chest X-ray.

Due to increasing difficulty in breathing and severe abdominal pain, we made a laparotomy by a median incision. Since the masses were originating from the ovarian region, we performed bilateral salpingo-oophorectomy and sent the masses to the frozen section analysis and 1,000 mL ascites was discharged (**Fig. 2**). Frozen section analysis reported a metastatic tumor of epithelial origin with areas of malignant adenocarcinoma.

Postoperative esophagogastroduodenoscopy revealed a fragile ulcerated area, 3 cm distal to the greater curvature corpus of the stomach, and a biopsy was taken. Pathological examination demonstrated signet ring cell adenocarcinoma metastasis in both ovaries and adenocarcinoma on gastric biopsy. The patient was transferred to the Medical Oncology Department on the 14th postoperative day. Cisplatin (CIS) and 5-fluorouracil (5-FU) treatment was

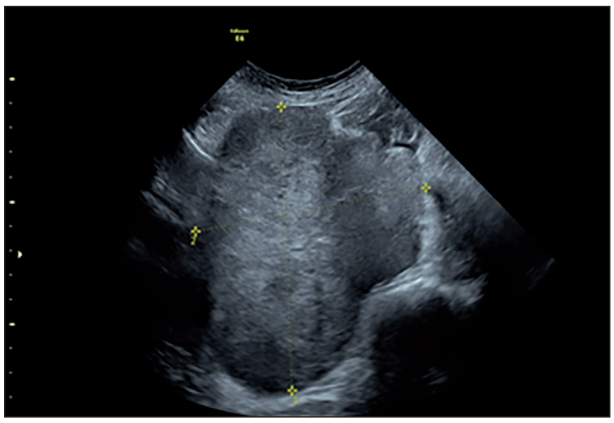

Figure 1. Ultrasonographic appearance of solid heterogeneous right ovarian mass.

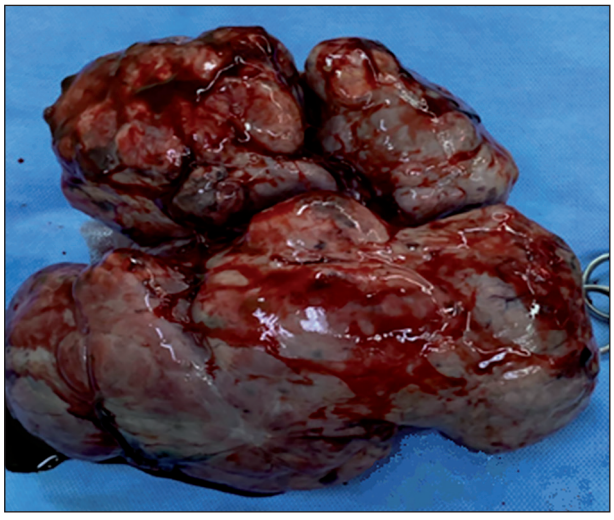

Figure 2. Macroscopic view of the ovarian mass.

started due to stage 4 gastric cancer. In the 30th week, she had contractions with cervical dilatation that did not respond to nifedipine tocolysis. The patient had a history of 2 previous cesarean deliveries and we performed a cesarean section after a course of betamethasone administration. A 1,070 g female baby with 1st and 5th minute Apgar scores of 8 was delivered.

After 2 CIS and 5-FU courses, paclitaxel treatment was started after tumor progression was observed on magnetic resonance imaging (MRI). The patient developed ileus and sepsis during the current treatment and died.

Case 2

A 33-year-old gravida 3, abortion 2 patient was consulted during the 20th week of pregnancy due to a diagnosis of gastric adenocarcinoma with an ovarian metastasis by the Medical Oncology Clinic. There was no history of cancer in her family history. It was learned that the diagnosis had been made at the beginning of the 2nd trimester at another institution. She had persistent nausea, vomiting, and abdominal pain. On the MRI examination at the 14th week, heterogeneous solid tumoral masses, a 15 cm mass on the right and a 10 cm mass in the left ovarian region, were detected with a live intrauterine fetus (**Fig. 3**), but no signs of metastasis were observed in the lungs or liver. Gastroscopy was performed and endoscopic biopsy revealed intestinal-type adenocarcinoma originating from the cardia region. She had a laparotomy at the 18th week in that institution, and a 15 cm sized mass had been removed from the right adnexal area. Since this operation was performed in an external center, we tried to find the reason for unilateral excision from the old epicrisis. Because of the difficulty in exploration due to pregnancy, and the invasion of surrounding tissues by the mass, we thought that extensive surgery was not performed. Pathological examination of the right salpingo-oophorectomy material had reported adenocarcinoma metastasis. After the family decided to continue the pregnancy, she was sent to our University Clinic for chemotherapy.

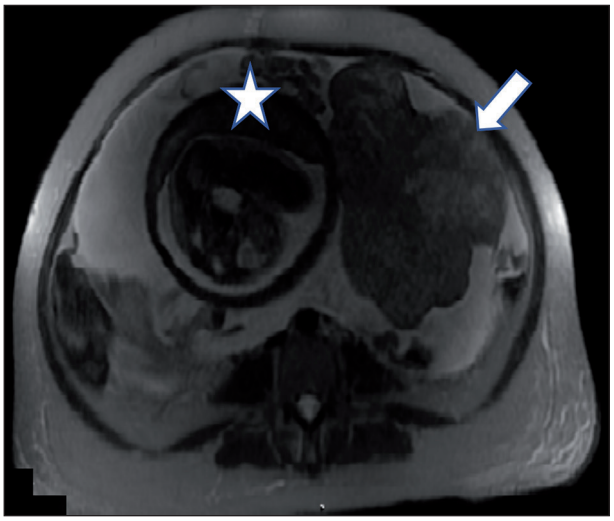

Figure 3. Fetus in the uterine cavity (white star) and a mass in the ovary (white arrow) observed on magnetic resonance imaging (MRI).

She had no obstetric problems; hemoglobin (8.3 g/dL), and platelet (22×10^4 µL) levels were low, but CA-125 (37 U/mL), CEA (7 ng/mL) were within normal limits. A healthy intrauterine fetus was observed on ultrasound, with no major structural anomalies, and a left-sided adnexal mass was confirmed. On MRI, there was a 10 cm left ovarian mass, and superior to this another mass of approximately 10 cm was visualized, but there was no metastasis in the liver or other intraabdominal organs. Chemotherapy with CIS and 5-FU was started at the 22nd week. Her pregnancy follow-up examinations were performed in our Clinic and were uneventful. At 29^{+4} weeks, when she received the 3rd cycle of chemotherapy, she had contractions with cervical dilation. We applied antenatal corticosteroids and magnesium sulfate for neuroprotective purposes. A cesarean section was performed due to breech presentation, and a 1,320 grams male fetus with respective 1st and 5th minute Apgar scores of 6 and 8 was delivered. An 18 cm mass on the left side of the abdomen, and omental cake were observed, and the intestines were conglomerated. Perioperative general surgery consultation was also called, but the case was considered inoperable. On the 5th postoperative day, the patient was transferred to the Medical Oncology Clinic. One month after the operation, positron emission tomography/computed tomography (PET/CT) revealed findings suggestive of tumors in the lungs and abdomen in the mesenteric and peritoneal areas, bilateral pleural effusion, and diffuse ascites in the abdomen. During the palliative treatment, the patient died 45 days after the operation in the Medical Oncology Service.

Discussion

Ovarian tumor during pregnancy is quite rare, with a reported incidence of 2.8-11 per 100,000 pregnancies [3, 4]. KT constitutes 1-2% of ovarian

tumors and they are considered advanced-stage ovarian tumors because of their different origins and poor prognosis. Most originate from the gastrointestinal tract, the commonest location being the stomach, followed by the colon, appendix, and breast [2, 5-8]. The stomach was also reported as the primary origin during pregnancy, as in both our cases [9, 10].

KT is one of the tumors that can cause virilization during pregnancy. Hirsutism was detected in approximately one-quarter of the cases [10], but in our patients, it was not observed. Diagnosis of these tumors during pregnancy is somehow difficult because symptoms such as nausea, vomiting, loss of appetite, and abdominal pain overlap with symptoms that ordinarily exist in a healthy pregnancy. Although it is not a common practice, it seems prudent to perform upper gastrointestinal endoscopy in pregnant women with persistent gastrointestinal symptoms and adnexal mass due to the possible risk of cancer [11, 12]. On the other hand, adnexal masses were also observed by imaging techniques in our patients. Solid masses of adnexal origin together with ascites and significantly elevated tumor markers raise the suspicion of ovarian carcinoma, mostly of epithelial origin, which must first be managed by surgery followed by chemotherapy. Thus, we have performed laparotomy in both cases. In case no. 2, mass excision and gastroscopy could not be performed during the same anesthesia application due to technical inadequacies. If this could be achieved, it would have been determined during the operation that the KT originated from the stomach and effective treatment could be performed. Effective management of KTs includes gastrectomy and metastasectomy. Wu et al. [8] reported that gastrectomy and ovarian metastasectomy in gastric tumors contributed positively to survival. Also, Peng et al. [13] stated that performing oophorectomy alone without primary resection in 133 patients who underwent ovarian metastasectomy due to gastric-induced tumors did not contribute to survival.

There are no adequate studies on endoscopy safety in pregnancy, and endoscopy during pregnancy has potential risks such as teratogenicity when performed during the 1st trimester or risk of preterm delivery in the 3rd trimester. Excessive sedation during the procedure may lead to maternal hypotension and hypoxia, but the fetus is very sensitive to these unfavorable situations [11]. In our cases, no procedure-related complications happened during or after endoscopy. The procedure can safely be performed by specialist endoscopists during pregnancy [12]. Due to the rapid progression of the tumor and even its worse prognosis in young people, the diagnosis should be made early. Therefore, endoscopy must be performed in cases with suspected adnexal malignancy despite the possible risks.

The prognosis of KTs varies: primary cancer originating from breast cancer has the best prognosis, whereas tumors of gastric origin have the worst prognosis [2, 6, 8]. The presence of ascites is also associated with an unfavorable prognosis. Kodama et al. reported that cases with respiratory and gastrointestinal symptoms have a worse prognosis, as in our patients [10-14]. While nausea, vomiting, and abdominal pain were prominent in both women, dyspnea was severe in our 1st case. Nausea and vomiting worsened gradually but, due to overlapping with the gastrointestinal complaints brought by pregnancy, were not taken seriously by the patient and the health staff, and severe respiratory distress developed.

Treatment of KT includes surgery and chemotherapy, depending on the primary tumor and its stage, but the ideal treatment protocol is unknown [5, 8, 10]. Identification of the primary tumor is essential for treatment planning [8]. In suitable patients, the primary treatment is surgery, and it contributes positively to survival [6, 15, 16]. Surgery can be performed when there are no distant metastases other than the ovary [13]. Due to the rapid progression of the tumor, surgery should be performed when the gestational week and stage are appropriate, and if radical surgery can be performed, it may contribute to survival [10]. Recent studies have proven that cytoreductive surgery, which includes resection of the primary lesion and ovarian metastasectomy, forms the basis of the treatment. The absence of macroscopic lesions after cytoreductive surgery increases survival [6, 8, 10, 13, 16]. On the other hand, as already said, another study stated that performing oophorectomy alone without primary tumor resection in gastric-induced tumors did not contribute to survival. Also, omitting gastrectomy in patients undergoing ovarian metastasectomy and the presence of ascites are independent risk factors associated with poor prognosis [13]. The mean overall survival of patients with KT related to gastric cancer was reported to be 11 months [8]. However, survival was poorer in our cases. Bilateral salpingo-oophorectomy without gastrectomy

was the procedure applied at the 25th and the 18th weeks in our cases, but patients died 3 months and 5 months after the diagnosis, respectively. Our cases support the fact that during pregnancy oophorectomy alone seems not to improve the survival. The lack of primary tumor resection in our cases may offer a possible explanation for the poor survival. Moreover, ascites might have also negatively affected the prognosis as previously suggested [13].

When KT is diagnosed in the 1st trimester of pregnancy, termination of pregnancy may be recommended to the family in order not to delay the treatment. However, if the family does not agree to termination, treatment should be postponed until after the 1st trimester due to the risk of abortion and malformation [17-19]. However, in our cases, the diagnosis was not made during the early period of pregnancy, but the 2nd patient and her family did not choose to terminate the pregnancy even after the diagnosis at the 18th week and postponed the chemotherapy until the 22nd week. Chemotherapy should be performed after the 1st trimester due to the risk of major congenital malformation and abortion [19]. The most appropriate approach and treatment options in the later weeks have been derived from existing studies, but the ideal treatment protocol remains unclear [18]. Platinum-based agents such as carboplatin, CIS, oxaliplatin, and 5-FU are commonly used in gastric-induced KT [6, 8, 18]. In our cases, chemotherapy was started as early as possible after the postoperative period but did not contribute to survival.

The most common obstetric complication in pregnancies complicated with cancer is preterm delivery [19, 20]. In a review including pregnant women with KT, the most common obstetric complication was also reported as preterm delivery [10], as in our cases; preterm delivery may have been triggered by common ascites and common intraabdominal disease.

Conclusion

In conclusion, since KT can occur at a younger age than other metastatic tumors of the ovary and early diagnosis should be offered to contribute to prognosis, the adnexal region should be checked routinely. It is easier to perform ultrasonographic evaluation of the adnexal area in the 1st trimester before the gestation progresses. Cases with persistent gastrointestinal symptoms together with an adnexal mass should be evaluated by gastroscopy.

Declaration of interest

The Authors declare that there is no conflict of interest.

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