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Vaginal cancer diagnosed during pregnancy presenting a therapeutic dilemma: A case report

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ABSTRACT

Background: Vaginal cancer is rare, accounting for only about 2% of all cancers of the female reproductive organs, and it is a disease that is rarely encountered in routine clinical practice. Vaginal cancer is mainly treated with radiation therapy or concurrent chemoradiotherapy (CCRT). However, in stage I-II cases, when the lesion is confined to the upper third of the vagina, surgical treatment may include total hysterectomy and vaginal resection with an adequate resection margin. We report a case of stage I vaginal cancer diagnosed at 13 weeks of gestation. There are very few reports on the diagnosis and treatment of vaginal cancer during pregnancy, and it was difficult to decide on a treatment plan; therefore, we report on the course of treatment followed for this patient.

Case presentation: The patient was a 38-year-old woman with a history of two pregnancies and zero births. The patient had thrombocytopenia and was diagnosed highly suspicious of myelodysplastic syndrome by bone marrow biopsy, and her platelet count remained at approximately 50,000/μL. At the time of the 11-week gestational checkup, a 4-cm pedunculated tumor was found in the right posterior vaginal fornix. Transvaginal tumor resection was performed at 13 weeks of gestation, and the patient was diagnosed with stage I vaginal cancer (squamous cell carcinoma). Because vaginal cancer was confined to the posterior vaginal wall fornix, radical surgery after abortion was suggested as a treatment plan. However, the patient strongly desired to continue the pregnancy, so the policy was to continue the pregnancy and follow-up. However, at 22 weeks of gestation, a recurrent tumor was found in the posterior fornix of the vagina. The lesion had invaded the paravaginal tissue, making radical surgery impossible. At 26 weeks of gestation, an elective cesarean section was performed because of giving priority to early therapeutic intervention to her recurrent vaginal cancer, and it was decided that CCRT with cisplatin would be administered from postpartum day 1. However, because of thrombocytopenia, chemotherapy could not be co-administered, and the treatment was completed with radiation alone. The therapeutic effect was partial response, but 13 weeks after the end of radiation therapy, we observed regrowth of the recurrent tumor and emergence of pelvic lymph node metastasis. The patient received palliative treatment but died 8 months after delivery due to a generally deteriorating condition, sepsis, and disseminated intravascular coagulation.

Conclusions: In cases of malignant tumors associated with pregnancy, treatment policies should consider the perinatal prognosis at the same time as treatment for malignant tumors, and gynecologic oncologists, obstetricians, and neonatologists, from the standpoint of their respective specialties, should thoroughly discuss the "curative effect of treatment for malignant tumors" and the "prognosis of the child after birth" and consider the treatment plan for each case.

1. Introduction

Vaginal cancer is a rare disease that accounts for only about 2% of all cancers of the female reproductive organs and is rarely encountered in routine clinical practice (Lilic et al., 2010). Because it is more common in the elderly and the majority of cases (80–90%) are squamous cell

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carcinoma, radiation therapy is generally the treatment of choice (Lilic et al., 2010). However, in stage I–II cases—which are confined to the upper third of the vagina—vaginal resection with a sufficient resection margin is considered in addition to total hysterectomy as surgical treatment (Saito et al., 2018).

Here, we report a case of stage I vaginal cancer diagnosed by transvaginal tumor removal at 13 weeks of gestation for a pedunculated tumor in the posterior vaginal fornix. There are very few reports on the diagnosis and treatment of vaginal cancer during pregnancy, and it was difficult to decide on a treatment plan; therefore, we report on the course of treatment followed for this patient.

2. Case

The patient was a 38-year-old female with a history of two pregnancies and no live births. This patient was referred to our hospital 9 weeks after pregnancy using assisted reproductive technology (ART) following fertility treatments. She had no abnormal findings on cervical cytology or pelvic examination prior to ART treatment. The patient had been under observation at the hematology department because of thrombocytopenia, which was suspected to be a complication of myelodysplastic syndrome diagnosed by bone marrow biopsy, Although the patient had no symptoms, the platelet count was approximately 50,000/μL.

At 11 weeks of gestation, the patient had a 4-cm pedunculated tumor in the right posterior vaginal fornix. Scraping cytology of the tumor surface revealed that the tumor was class V (malignant cell), and pelvic magnetic resonance imaging (MRI) performed at 12 weeks of gestation showed a 4-cm mass with low intensity on T1-weighted images and high intensity on T2-weighted images in the same area (Fig. 1). Whereas her uterine cervix is normal finding on inspection, and the result of PAP test was negative. Based on these findings, we suspected vaginal cancer, and transvaginal tumor resection was performed at 13 weeks of gestation to confirm the diagnosis. The surgery was performed under general anesthesia: the peduncle of the hemorrhagic tumor growing from the right posterior vaginal fornix was pinched and ligated, and the tumor was removed as a single mass. The pathological diagnosis of the excised tumor was squamous cell carcinoma (Fig. 2). Venous invasion was positive, but the resection margins were negative. On examination, the tumor was confined to the vaginal wall without extension to the portio vaginalis, vulva, or paravaginal tissue, and was therefore diagnosed as stage I vaginal cancer.

Initially, the obstetrician in charge of the patient thought that they could continue with the pregnancy because the cancer was limited to the posterior vaginal fornix and had been completely resected. However, the gynecologic oncologist who was consulted judged that radical surgery was necessary because of vascular invasion. At 15 weeks of gestation, the obstetrician and gynecologic oncologist discussed the possibility of performing a radical hysterectomy, vaginal resection, and pelvic lymph node dissection after abortion as a subsequent treatment plan. However, the patient and their family wished to continue the pregnancy because the pregnancy had been conceived after infertility treatment, and they could not accept the proposed treatment plan. Another option was to continue the pregnancy while giving chemotherapy, but due to the low platelet levels, we decided that chemotherapy would be difficult for her Therefore, it was decided that the patient would continue with the pregnancy and be monitored.

At 22 weeks of gestation, a rapidly growing recurrent tumor was found in the posterior vaginal fornix, and pelvic MRI performed at 25 weeks of gestation showed that the growing tumor had spread from the right paravaginal tissue to the pelvic wall (Fig. 3A). It was determined that radical surgery was impossible. We decided that the pregnancy would be promptly terminated, and the patient would receive radical radiation therapy. After administration of betamethasone for 2 days to promote lung maturation of the fetus, an elective cesarean section was performed at 26 weeks and 2 days of gestation for the early start of the mother's treatment. The infant was born with a birthweight of 890 g, Apgar score of 4/6, and survival without sequelae. Initially, concurrent

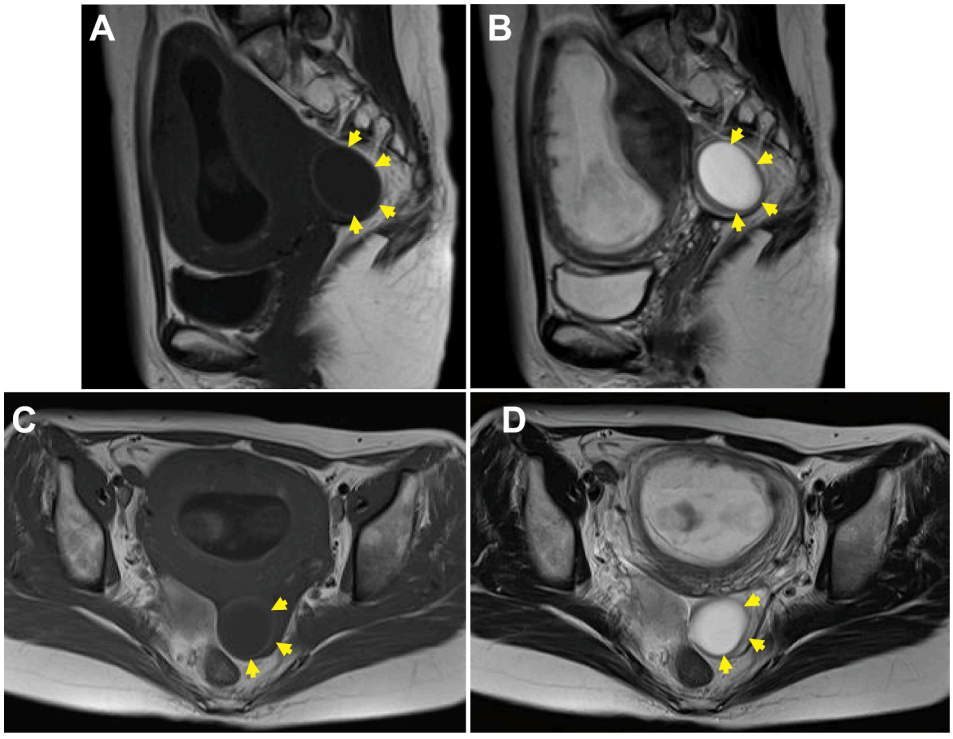

Fig. 1. Magnetic resonance imaging at 12 weeks of gestation. A) T1-weighted sagittal image. B) T2-weighted sagittal image. C) T1-weighted axial image. D) T2-weighted axial image. Arrows show a 4-cm tumor in the posterior fornix with low intensity on T1-weighted imaging and high intensity on T2-weighted imaging.

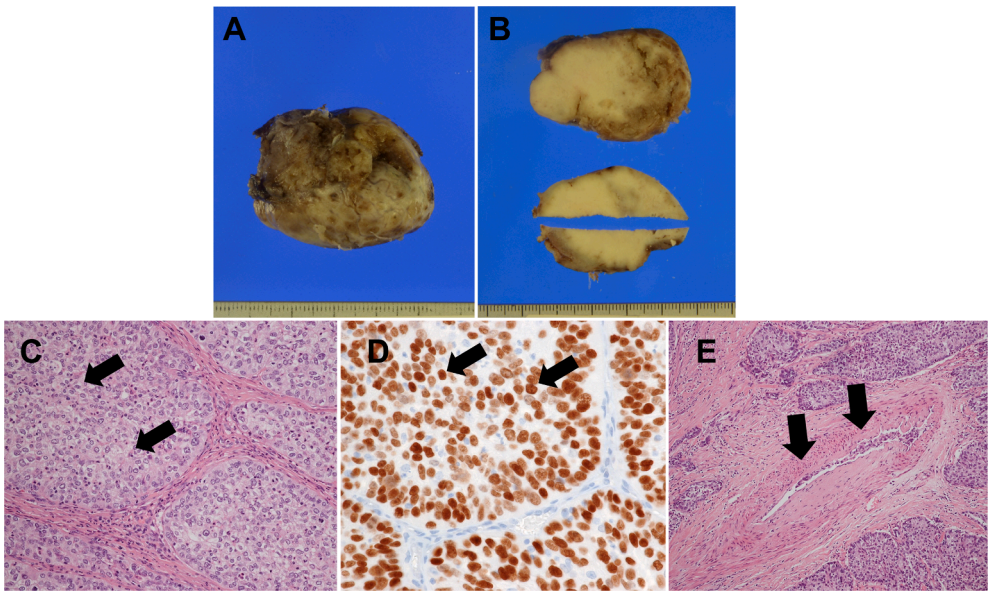

Fig. 2. Histopathological findings of the tumor. A) and B) Macroscopic findings of vaginal tumor (45 mm × 35 mm × 30 mm, 30 g). The tumor was slightly soft with no necrosis or intratumoral hemorrhage. C) Hematoxylin and eosin (H&E) staining showing squamous cell carcinoma, non-keratinizing type (×200). D) Immunohistochemical staining showing p40 positive cells (×400). E) H&E staining showing venous invasion (×100).

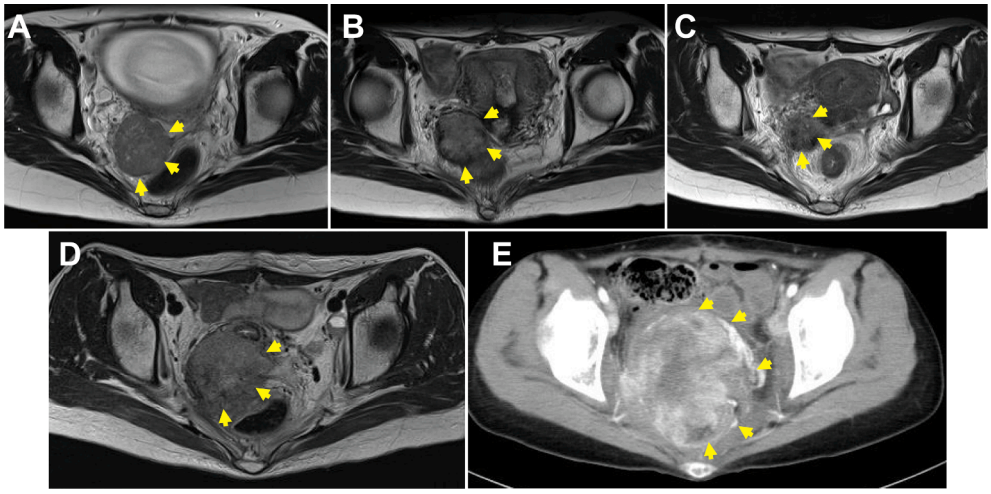

Fig. 3. Time-series changes in magnetic resonance imaging (MRI) and computed tomography (CT). A) MRI T2-weighted axial image (25 weeks of gestation). B) MRI T2-weighted axial image (4 weeks postpartum). C) MRI T2-weighted axial image (12 weeks postpartum). D) MRI T2-weighted axial image (22 weeks postpartum). E) Contrast-enhanced CT (27 weeks postpartum). Arrows show change in tumor size. Partial response was achieved by radiotherapy (C), but the tumor promptly recurred (D). Rectum permeation finally developed, and the bleeding from the anus lasted (E).

chemoradiotherapy (CCRT) with cisplatin was planned, but it was judged that concurrent chemotherapy was difficult due to thrombocytopenia, and radiation alone (external beam: 60 Gy/30 Fr) was started on postpartum day 10. There were no adverse events during treatment, and the treatment was completed as scheduled.

While radiological assessments conducted 3 weeks after the end of radiation therapy suggested partial response, the recurrent tumor increased in size 13 weeks after the completion of radiation therapy and pelvic lymph node metastasis was observed (Fig. 3D). Eighteen weeks after the completion of radiation therapy, rectal invasion was also observed and vaginal and transrectal bleeding from the recurrent tumor continued, so transfusion therapy was continued (total red blood cells, 16,520/mL, platelets, 4,700/mL). Colostomy construction was also performed to ensure oral nutrition and control bleeding, since there was a tendency for increased vaginal bleeding during defecation due to rectal invasion, but bleeding from the tumor was continued. Due to thrombocytopenia, it was difficult to administer second-line chemotherapy. After palliative treatment, the patient died 13 months after the initial treatment and 8 months after delivery due to deterioration of general condition, sepsis, and disseminated intravascular coagulation.

3. Discussion

Because squamous cell carcinoma is the predominant histological type of vaginal cancer, and because it is more common in the elderly, radiotherapy is often the treatment of choice (Saito et al., 2018). Although in stage I–II cases of vaginal cancer confined to the upper third of the vagina, surgery has a better prognosis than radiation therapy (Saito et al., 2018; Stock et al., 1995; Tabata et al., 2002; Creasman et al. 1998; Tjalma et al. 2001), the survival rate in stage I vaginal cancer has been reported to be better with surgery plus radiation therapy, surgery alone, and radiation therapy alone (Di Donato et al., 2012). For this reason, surgical treatment is considered for stage I–II patients with disease confined to the upper third of the vagina. If surgical treatment is chosen, a vaginal excision with sufficient margins to remove the vaginal wall is generally performed along with a quasi-extensive or extensive

total hysterectomy, as in cervical cancer, with additional pelvic lymph node dissection.

This was a case of stage I vaginal squamous cell carcinoma in early pregnancy. Because of the localization of the tumor, radical surgical treatment after abortion was suggested, but the patient refused radical treatment and continued the pregnancy. After delivery of the baby by cesarean section at 26 weeks of gestation, radiation therapy was administered. However, the tumor reappeared after the completion of treatment, metastasizing to the pelvic lymph nodes and invading the rectum, and the patient's general condition deteriorated, resulting in death.

There have been very few reports of vaginal cancer associated with pregnancy, with only 14 cases reported so far (Fujita et al., 2005; Xu et al., 2020). In this study, we investigated 15 cases of pregnancy-associated vaginal cancer, including the present case. According to the stage of disease progression, 9 cases (60.0%) were stage I, 6 cases (40.0%) were stage II. By histology, 14 cases (93.3%) were squamous cell carcinoma and 1 case (6.7%) was adenocarcinoma. The adenocarcinoma case was a stage I clear-cell carcinoma (Xu et al., 2020). Of the 8 stage I squamous cell carcinoma cases, 3 pregnancies ended before 22 weeks of gestation (1 spontaneous miscarriage and 2 abortions for treatment of vaginal cancer). One case of spontaneous miscarriage went into remission with radiation therapy and did not recur, while the two cases of abortion died of cancer progression or recurrence. However, all 5 patients who continued their pregnancies after 22 weeks of gestation achieved a live birth by cesarean section, but 2 patients, including this patient, died from progression or recurrence of cancer. In general, the 5-year survival rate for stage I vaginal cancer is 70–80% (Kirkbride et al., 1995; Kucera et al., 2001). However, 4 of 8 cases (50.0%) of stage I vaginal squamous cell carcinoma associated with pregnancy were found to have died of cancer, indicating a poorer prognosis than in non-pregnant cases. While delay in the start of treatment due to continuation of pregnancy may lead to poorer prognosis in cases associated with pregnancy, two of the four fatal cases in this study started treatment early due to abortion, suggesting that there may be other factors (e.g., the effect of the pregnancy environment on the tumor) that contribute to a poor prognosis in cases of pregnancy. However, due to the small number of cases, it is not possible to speculate any further.

The decision to treat vaginal cancer diagnosed during pregnancy requires multidisciplinary management that considers a variety of influencing factors, including the impact of treatment on the mother and fetus and ethical factors, in addition to the oncologic prognosis (Soo-Hoo and Luesley, 2016). If diagnosis is made at a gestational age when the fetus can survive outside the uterus, radical treatment should be initiated as soon as possible after delivery of the baby. However, if the diagnosis is made at a gestational age when the fetus is not viable outside the uterus, the prognosis of the mother should be given the highest priority, and careful consideration should be given to the stage of disease progression and gestational age, as well as the wishes of the patient and family.

This was a case of vaginal carcinoma that grew in a pedunculated manner, and complete resection was possible at the early stage of pregnancy. However, the pathological findings of the resected specimen showed vascular invasion, and considering the risk of recurrence, it was suggested that the patient undergo radical surgery after early pregnancy interruption. However, the patient and their family did not accept the treatment plan we proposed because pregnancy had been achieved by ART. Given the background of the pregnancy, it is natural that the patient had difficulty accepting the idea of interrupting the pregnancy, but it is extremely important to provide objective information on the impact of continued pregnancy on cancer prognosis, specifically on the predicted worsening of oncological prognosis due to a delay in the initiation of curative treatment.

4. Conclusion

We encountered a very rare case of vaginal cancer diagnosed during pregnancy. In cases of malignant tumors associated with pregnancy, it is necessary to consider the perinatal prognosis as well as the treatment of the malignant tumor. Especially, in situations such as the present case, even though the patient strongly desires to continue the pregnancy, gynecologic oncologists, obstetricians, and neonatologists should thoroughly discuss the "curative effect of treatment for malignant tumors" and the "prognosis of the child after birth" from the standpoint of their respective specialties, and should consider the treatment plan objectively.

Ethics approval and consent to participate

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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CRediT authorship contribution statement

Koki Samejima: Writing – original draft. **Tomonori Nagai:** Project administration. **Yuichiro Kizaki:** Investigation. **Kosuke Shigematsu:** Investigation. **Yoshiko Kurose:** Investigation. **Takahiro Uotani:** Data curation. **Taichi Akahori:** Data curation. **Yasushi Takai:** Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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