Successful spontaneous pregnancy in a patient with rectal carcinoma treated with pelvic radiotherapy and concurrent chemotherapy: the unique role of laparoscopic lateral ovary transposition

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Summary

Concurrent administration of external beam pelvic radiotherapy (RT) and chemotherapy (CT) is an effective treatment modality for rectal cancer. In adults in reproductive age, one of the most important side-effects resulting from this treatment is gonadal toxicity. Fortunately, it is possible to protect the ovaries by transporting them out of the RT area through lateral ovary transposition (LOT), as a minimally invasive method, which is performed before the application of RT. A 24-year-old female was diagnosed as having rectal adenocarcinoma in May 2003, and she was scheduled to receive adjuvant 5-fluorouracil-based CT followed by concurrent chemoradiotherapy (CRT). Before the onset of the adjuvant treatments, laparoscopic LOT was performed, and the patient was followed-up appropriately. Although amenorrhea developed during the CRT, the menstrual cycle of the patient resumed without performing any medical treatment eight weeks after the completion of the CRT. In July 2005, the patient became pregnant spontaneously with no local or systemic recurrences of rectal cancer. The present case shows that ovarian functions can be successfully protected in rectal cancer patients receiving RT by laparoscopic LOT, and by modifying the RT fields.

Key words: Rectal carcinoma; Laparoscopic ovary transposition; Pelvic radiotherapy.

Introduction

External-beam radiotherapy (EBRT) is used for the definitive treatment of various pelvic tumors. Generally, a total of 45 Gy is given to the whole pelvis with 1.8-2 Gy daily fractions, which is followed by increasing doses to the primary tumor bed. In case the gonads are not preserved, premature ovarian failure, infertility, and early menopause are commonly encountered during irradiation of the rectal cancer by the pelvic box technique. To preserve fertility and to prevent medical castration, medial or lateral ovary transposition (LOT) is commonly employed in premenopausal individuals with Hodgkin's disease and gynecologic malignancy [1, 2]. Other methods such as cryopreservation and transplant of the ovarian tissue have been stated to be effective in patients receiving pelvic radiotherapy (RT) [3]. However, ovary transposition has gained an important place for the preservation of fertility and ovarian function in patients receiving pelvic RT. Interestingly, the role of ovary transposition performed by the laparoscopic approach, as a fertility-preserving treatment, is not entirely documented in patients with rectal cancer, who are commonly treated with RT with or without chemotherapy (CT). In a few reports, laparoscopic ovarian transposition was found to be an effective approach preserving fertility among rectal cancer patients after pelvic RT [4].

In this report, we present a case with locally advanced rectal cancer, that demonstrated preserved fertility and who become pregnant after concurrent pelvic EBRT and CT by the use of LOT.

Case Report

A nulligravid, 24-year-old woman was admitted to the Oncology Clinic of Uludag University Medical School with the main complaint of rectal bleeding which started in March 2003. Rectosigmoidoscopy revealed a rectal ulcerated lesion that was pathologically diagnosed as adenocarcinoma. Examinations did not show distant metastasis, and the patient underwent low anterior resection on May, 2003. Pathological examinations revealed T3N1 rectal adenocarcinoma according to the standard TNM classification. Then, laparoscopic LOT was performed on the patient, who had been demonstrated to have normal ovarian function by appropriate laboratory tests (clomiphene citrate challenge test, CCCT), four weeks after the operation. By this procedure, the right and left ovaries were fixed to the right and left antero-lateral paracolic areas, respectively, and the lower borders of both ovaries were marked with endoclipses. The patient was then administered two cycles of adjuvant CT consisting of 5-fluorouracil (5-FU) 425 mg/m^2/day plus calcium leucovorin 20 mg/m^2/day, which were given for five consecutive days of every 28 days followed by concurrent CRT comprised of EBRT (50.4 Gy, 1.8 Gy/day fractions) and 5-FU (300 mg/m^2/day as continuous infusion for five days a week during

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the course of RT). The RT fields were modified, and applied as asymmetric-centered to two lateral areas. The RT planning was made by using the abdominopelvic computerized tomography sections. The asymmetric center was placed 2 cm behind the ovaries, and an initial 45 Gy radiation dose was given with 25 MV photon energy using two lateral fields. Then, a 5.4 Gy boost dose was applied using anterior- posterior fields bringing the total dose to 50.4 Gy. After CRT, two cycles of 5-FU plus calcium leucovorin were administered with the same doses and schedule as given before CRT.

During CRT, the right and left ovaries were exposed 3.87 Gy (8.2% of the total dose) and 7.45 Gy (15% of the total dose) irradiation doses, respectively (Figure 3). After the completion of RT, ovarian function was followed by clinical findings and laboratory tests. The results concerning the ovarian function before and after RT are summarized in the Table 1. The patient experienced her last menstruation in May 2005, and applied to our hospital with the chief complaint of delayed menstruation on June, 2005. By US, a single live intrauterine fetus was detected. The ovaries were observed at the location where they were placed by oophoropexy. The pregnancy continued without any problem during the initial 20 weeks. However, *in utero* exitus developed at the 21st week of the pregnancy. The patient has continued normal menstrual cycles, and has been followed on a regular basis.

Table 1. — *Effect of chemoradiotherapy on ovarian function.*

	Before RT-Baseline (3rd day)	Before RT-CCCT (8th day)	After RT-Baseline (3rd day)	After RT-CCCT (8th day)
FSH (mIU/ml)	6.81	11.20	20.12	8.38
LH (mIU/ml)	12.47	14.22	12.58	12.04
Estradiol (pg/ml)	28.3	45.80	42.7	381.1

RT: Radiotherapy, CCCT: Clomiphene citrate challenge test.

Discussion

Radical surgical resection and pre- or postoperative CRT are the standard treatments of locally advanced rectal carcinoma. However, CRT negatively affects the reproductive functions of the patients. The estimated irradiation dose required to destroy 50% of human oocytes (LD_{50}) is < 2 Gy [5]. Ovarian failure is seen in almost all females who received 20-30 Gy whole abdominal RT in childhood [6, 7]. Ovarian transposition is an effective and safe modality for protecting ovarian functions in women in reproductive age, who are scheduled to receive pelvic RT [1,2,4). By the use of LOT, 88.6% of cases showed preserved ovarian function after RT [8]. For our patient, the right and left ovaries were exposed to 3.87 Gy (8.2% of the total dose) and 7.45 Gy (15% of the total dose) irradiation doses, respectively. Although the exposed doses were associated with some degree of oocyte loss, we observed that the ovaries could be considerably protected against irradiation-induced injury, and the ovarian function and fertility could be successfully preserved by laparoscopic LOT.

An important factor influencing fertility in patients receiving RT is the tolerance of the uterus to irradiation, which varies depending on the total RT dose and the RT area. It was stated that the irradiation doses of 14-30 Gy may cause uterine dysfunction [9, 10]. However, endometrial activity may be maintained after relatively higher irradiation doses. In this situation, pregnancy may occur, but adverse pregnancy outcomes including early pregnancy loss, preterm birth, and fetal growth retardation are more common due to the irradiation-induced changes in the endometrium and myometrium as well as in uterine blood flow [11, 12]. Our case was treated with a relatively high dose of postoperative pelvic RT (50.4 Gy) concurrently with 5-FU at a dose of 300 mg/m^2, and she was shown to have preserved ovarian function and could become pregnant by the use of LOT prior to the treatments and by modifying the RT fields. However, *in utero* exitus developed at the 21st week of the pregnancy. The above-mentioned data as well as our case shows that fertility could be preserved after high-dose pelvic RT by LOT, but adverse pregnancy outcomes may possibly occur due to the RT-induced changes on the uterus.

The information regarding the efficacy of ovarian transposition to preserve fertility against the harmful effects of RT in rectal cancer is extremely limited. Tulandi *et al.* [13] showed the effectiveness of laparoscopic LOT on the preservation of ovarian function in a patient with rectal adenocarcinoma. Similarly, Farber *et al.* [4] reported a case with rectal cancer preserving ovarian function by laparoscopic ovarian transposition. In the latter case report, the authors concluded that ovarian transposition should be considered in abdominal and pelvic malignancies before the application of RT, if the patient desires to continue fertility. This fact was delineated in another manuscript, and laparoscopic ovary transposition was thought to be an underused procedure, in spite of its efficacy and simplicity [8]. These previous reports and our case imply that laparoscopic LOT should be offered to young rectal cancer patients who desire preservation of ovarian function.

In conclusion, we showed that fertility could be preserved and a successful pregnancy can occur after a relatively high dose of pelvic RT via laparoscopic LOT. Modifying the RT fields without any detrimental effect on its efficacy yields an additional impact on the success of the surgical approach. However, clinicians should be aware of the possible occurrence of adverse pregnancy outcomes.

References

[1] Bisharah M., Tulandi T.: "Laparoscopic preservation of ovarian function: an underused procedure". *Am. J. Obstet. Gynecol.*, 2003, *188,* 367.

[2] Tinga D.J., Dolsma W.V., Tamminga R.Y., van der Zee A.G.: "Preservation of ovarian function in 2 young women with Hodgkin disease by laparoscopic transposition of the ovaries prior to abdominal irradiation". *Ned. Tijdschr. Geneeskd.*, 1999, *143,* 308.

[3] Newton H., Aubard Y., Rutherford A., Sharma V., Gosden R.: "Low temperature storage and grafting of human ovarian tissue". *Hum. Reprod.*, 1996, *11,* 1487.

[4] Farber L.A., Ames J.W., Rush S., Gal D.: "Laparoscopic ovarian transposition to preserve ovarian function before pelvic radiation and chemotherapy in a young patient with rectal cancer". *Med. Gen. Med.*, 2005, *7,* 66.

[5] Wallace W.H., Thomson A.B., Kelsey T.W.: "The radiosensitivity of the human oocyte". *Hum. Reprod.*, 2003, *18,* 117.

[6] Wallace W.H., Shalet S.M., Hendry J.H., Morris-Jones P.H., Gattamaneni H.R.: "Ovarian failure following abdominal irradiation in childhood: the radiosensitivity of the human oocyte". *Br. J. Radiol.,* 1989, *62,* 995.
[7] Wallace W.H., Shalet S.M., Crowne E.C., Morris-Jones P.H., Gattamaneni H.R.: "Ovarian failure following abdominal irradiation in childhood: natural history and prognosis". *Clin. Oncol.* (R. Coll. Radiol.), 1989, *1,* 75.
[8] Bisharah M., Tulandi T.: "Laparoscopic preservation of ovarian function: an underused procedure". *Am. J. Obstet. Gynecol.,* 2003, *188,* 367.
[9] Critchley H.O.D., Wallace W.H.B., Shalet S.M., Mamtora H., Higginson J., Anderson D.C.: "Abdominal irradiation in childhood: the potential for pregnancy". *Br. J. Obstet. Gynaecol.*, 1992, *99,* 392.
[10] Bath L.E., Critchley H.O., Chambers S.E., Anderson R.A., Kelnar C.J., Wallace W.H.: "Ovarian and uterine characteristics after total body irradiation in childhood and adolescence: response to sex steroid replacement". *Br. J. Obstet. Gynaecol.*, 1999, *106*, 1265.
[11] Hammer R.A., Urnes P.D., Lurain J.R.: "Unanticipated pregnancy with intrauterine growth retardation after radiation-induced ovarian failure. A case report". *J. Reprod. Med.,* 1996, *41,* 372.
[12] Critchley H.O.,Wallace W.H.: "Impact of cancer treatment on uterine function". *J. Natl. Cancer Inst. Monogr.,* 2005, 64.
[13] Tulandi T., Al-Took S.: "Laparoscopic ovarian suspension before irradiation". *Fertil. Steril.*, 1998, *70,* 381.

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