

Female Fertility Preserving and Gonadal Protection in Patient with Colorectal Cancer

Abstract

One of the most common malignancy of the gastrointestinal tract is the colorectal cancer. Recently, the incidence of colorectal cancer in young patients is higher and very often these patients are women. These patients can necessitate the use of chemotherapy and/or radiation therapy. For this reason it is very important that physicians discuss about the risks of infertility and methods of fertility preservation before any intervention. In the present case the patient was undergoing to laparoscopic ovarian transposition and oocytes aspiration obtained transvaginally in the same surgical session, avoiding a second surgery. By using combined fertility preservation it is possible to offer the patient different treatments using only one surgical procedure and probably increasing the chance to achieve pregnancy.

Case Report

Volume 2 Issue 6 - 2015

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Received: May 21, 2015 | **Published:** October 6, 2015

Introduction

The colorectal cancer (CRC) is the most common malignancy of the gastrointestinal tract. The majority of colorectal cancers are diagnosed after the age of 55. The incidence of CRC in patients under the age of 40 is 8% [1,2] and 3-6% in patients between 20 and 40 year-old. Nearly 48% of these patients are women [3,4]. It was identified an increased incidence of rectal cancer in patients aged less than 40 years, between 1973 e 2005, with an estimated incidence of 4% according to US database [2] and about 2% according to European database [5]. Younger patients seem to have a higher incidence of histologically aggressive tumors and distant metastases with a recurrence rate of 20% and a significantly worse 5-years survival rate (38%), compared with older patients [5].

These patients can necessitate the use of chemotherapy, radiation therapy or a combination of both [6]. For this reason it is essential that physicians discuss about the risks of infertility and methods of fertility preservation before any intervention because all the procedures may compromise the function of one or more parts of the reproductive system [7]. Chemotherapy induced damage to the ovarian structures with different results. The cytotoxic effects depend on age, treatment protocol, type and dose of chemotherapeutic agent. The standard 5-FU based chemotherapy may have mild or no gonadotoxic potential effects on female fertility [1]. Radiation therapy is an important adjuvant treatment in rectal cancer and preoperative administration has improved rates of local control [8]. The use of radiotherapy can result in the loss of ovarian function because human oocytes are extremely sensitive to radiation with an estimated dose of 20 Gy sufficient to cause permanent ovarian failure. The degree of damage is dependent on the age at time of therapy, dose and field of irradiation. The uterus is also susceptible to damage

by radiation therapy with possible obstetric complications if pregnancy is achieved [1,9,10].

There is a lack of studies examining the effect of surgery for rectal cancer on female fertility [4]. In particular there is conflicting evidence on the fact that open surgery would result in a greater impact on fertility compared with the laparoscopic approach. Probably laparoscopic procedures would result in fewer adhesions with less disruption to the peritoneum. At the present the most appropriate fertility preservation strategies are ovarian transposition, ovarian tissue and oocytes or embryos cryopreservation. Laparoscopic ovarian transposition is realized placing the ovaries above the pelvic brim and as lateral as to place them outside the radiation field with preservation of fallopian tubes allowing a possible future spontaneous conception [11]. This technique is simple, effective and allows the spontaneous repositioning of the ovary with no disruption of anatomical relationship to the other organs.

In women younger than 40 years the laparoscopic ovarian transposition is associated with preservation of ovarian function in 88,6% of the cases [11]. In fact it is estimated that the dose of radiation to the transposed ovaries is reduced by approximately 90% to 95% compared to their normal pelvic position [4]. Several options are available to females with rectal cancer who wish to preserve their reproductive potential. Embryo cryopreservation is the most successful technique with a pregnancy rate of 20% to 30% per transfer of 2 or 3 embryos [12]. Some authors reported a cumulative pregnancy rate of 60% when multiple embryos are available [1,10]. The prerequisites for embryos cryopreservation are the availability of a fertile male partner or donor sperm and ovarian stimulation with delay of cancer treatment. Oocytes cryopreservation is a possible option for patients with no male partner and in 2012 became standard therapy for patients

without a partner or who elected not to use donor sperm or freeze embryos. New cryopreservation technique as vitrification have greatly improved the survival rate of oocyte after thawing with viable pregnancies [13,14].

Case Report

In 2010 a 37 year-old woman with a diagnosis of rectal adenocarcinoma (pT2N1a) underwent previous ileostomy in anterior resection of the rectum. Biopsy and istological examination of the mass revealed a moderately differentiated intestinal adenocarcinoma, ulcerated, that invades the muscular propria with an infiltrative growth. No evidence of peritumoral vascular invasivity was reported. Dworak regression: grade 1 (range 0-4). She required pelvic irradiation and chemotherapy. In particular it was proposed an adjuvant FOLFOX (5-fluorouracil, leucovorin and oxaliplatin) chemotherapy that represents the most widely used standard treatment for rectal cancer. Due to the young age of the patient, it was very important to discuss fertility risks associated with cancer treatment and all the options available for fertility preservation. She went to our Clinic for fertility preservation. She underwent in 28th cycle day a first transvaginal ultrasound with detection of polycystic ovaries and with the finding of a major follicle of 16 mm diameter. Ultrasound data is consistent with menstrual irregularities. So it was offered a program of ovulation induction in the luteal phase with both gonadotropins (Meropur 75IU/day) and cetrorelix 0.25 (Cetrotide 1fl sc/day) for oocytes cryopreservation, before to perform oophoropexy.

Therefore it was proposed to proceed simultaneously in cryopreservation and oophoropexy in the same operative session. After the procedures were explained to her, she accepted and signed an informed consent form. The first stage of surgery was a transvaginal ultrasound guided for follicular aspiration. There were picked up 19 oocytes, 10 from the left ovary and 9 from the right one. She cryopreserved 5 oocytes with slow freezing procedures and 3 embryos. At time of cryopreservation the slow freezing was an established technique in the center with good implantation rate (about 18%) and at the time, vitrification was still not performed routinely. Semen parameters were normal following the indication of WHO 1999. The second surgical stage was laparoscopic oophoropexy with a standard technique previously described by many authors [15].

Both procedures were performed rapidly with one hour and thirty minutes of total duration. Later the patient underwent surgery with post surgical complications and was discharged after five months of hospitalization then the patient underwent chemoradiotherapy with poor health conditions. Due to this, the follow-up routinely performed at 6 months was not performed.

Discussion

In this report we investigated the feasibility and safety of the laparoscopic ovarian transposition and transvaginal retrieval of mature oocytes during the same surgical session. Both laparoscopic ovarian transposition and oocytes aspiration were carried out as standard procedures because they represent the

fertility preservation preferred options for women with colorectal cancer before pelvic irradiation. We described the possibility to provide two different treatments using only one surgical procedure. Technically, we performed the procedures under only one general anesthesia instead of two, that means a decreased physical and emotional distress for the patient.

Moreover, another important issue regarding women with colorectal cancer is often the lack of time available to clinicians and patients to discuss about fertility preservation options and to choice the better treatment. We believe that combining ovarian transposition with oocytes retrieval, reducing the duration of the surgery before pelvic irradiation, could be a potential treatment to maximize chances for future fertility.

Given the increased incidence of colorectal cancer and high risk for treatment-induced infertility, it is very important to perform an adequate reproductive counseling. It is also important to emphasize how the overall 5 years survival rate is increased over the past 20 years from 50 to 64% by allowing patients to reach childbearing age [8]. Unfortunately it is estimated that only 47% of US physicians are following the guidelines from the American Society of Clinical Oncology, which suggest that all patients of childbearing age should be informed about fertility preservation [7,16]. In particular only 15% of women aged 18-45 years with colorectal cancer received pretreatment fertility counseling [17].

Very few little data exist in the literature for utilizing a multidisciplinary approach to offer a solution for female fertility preservation. However, nowadays significant advances are allowing women to preserve their fertility after cancer treatment. For this reason, performing these concomitant standard procedures could be, in our opinion, an important extra opportunity for these patients.

Conclusion

In the present case the patient was given the opportunity to perform a double treatment in the same surgical session, avoiding to the patient a second surgery. It was decided to perform laparoscopic ovarian transposition and oocytes aspiration obtained transvaginally under ultrasound guidance. This is a relative easy and safety procedure and compared with laparoscopy the vaginal approach resulted in a higher oocyte recovery rate, shorter surgery time, a superficial anesthesia and a less invasive technique [18]. Furthermore adverse effects on embryo development may occur following exposure to carbon dioxide (CO₂) used to create pneumoperitoneum, which is known to cause a decrease in Ph follicular fluid. A reduction in pH may affect fertilization and early embryonic development. Moreover CO₂ exposure may affect fertilization with no effect on the rate of cleavage of the embryos [19].

By using combined fertility preservation it is possible to offer the patient different treatments using only one surgical procedure and probably increasing the chance to achieve pregnancy. At the time of this writing the patient didn't have any pregnancy and she's waiting for surgery for correction of vagino rectal fistula.

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