



Ovarian transposition and metachronous ovarian metastasis in a premenopausal colorectal carcinoma patient: a case report

Shari Bodofsky¹^, Sean Hong¹, George N. Botros¹, Evita Sadimin²^, Patrick M. Boland³, Matthew P. Deek¹^

¹Department of Radiation Oncology, Rutgers Cancer Institute of New Jersey, Rutgers University, New Brunswick, NJ, USA; ²Department of Pathology and Laboratory Medicine, Rutgers Cancer Institute of New Jersey, Rutgers University, New Brunswick, NJ, USA; ³Department of Medical Oncology, Rutgers Cancer Institute of New Jersey, Rutgers University, New Brunswick, NJ, USA

Correspondence to: Shari Bodofsky. Department of Radiation Oncology, Rutgers Cancer Institute of New Jersey, Rutgers University, 195 Little Albany Street, New Brunswick, NJ 08903, USA. Email: sb1566@rwjms.rutgers.edu.

Abstract: Colon cancer has a high incidence of metastasis, with an estimated 0.8–7.4% of colorectal adenocarcinoma (CRC) cases metastasizing to the ovary. The role of prophylactic bilateral oophorectomy in CRC is contested in the literature, particularly in premenopausal patients. Further, it is unclear if prophylactic removal of the contralateral ovary is indicated in cases of direct involvement of one ovary to reduce recurrence. Facing a lack of evidence for survival benefit, hormonal complications, and sterilization, some choose to pursue fertility sparing options. For female patients interested in additional pregnancies, the ovaries can be surgically relocated in a prophylactic procedure known as ovarian transposition; as even small doses of radiation to the ovary can effectively sterilize women in their 30 s. We present a case of a 29-year-old female who underwent ovarian transposition of the right ovary before initiating chemoradiation for primary left sided colon adenocarcinoma with direct invasion of the left ovary. Months later, she presented to the emergency department (ED) with abdominal pain suspicious for ovarian torsion. On restaging computerized tomography (CT), she was diagnosed with symptomatic right ovarian metastasis in the transposed ovary, requiring reoperation and oophorectomy. For this patient, and for others facing critical decisions about ovarian preservation in advanced colorectal cancer, the question remains how to balance fertility concerns with optimal minimization of metastasis and recurrence.

Keywords: Ovarian transposition; prophylactic oophorectomy; ovarian metastasis; case report

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Introduction

Colon cancer has a high incidence of metastasis, with 20% of patients presenting with Stage IV disease at diagnosis (1). Common sites of metastasis include the lymph nodes, liver, lungs, and peritoneum. An estimated 0.8–7.4% of colorectal adenocarcinoma (CRC) cases metastasize to the ovary, with even higher rates discovered postmortem at 5–9.7% (2). Additionally, an estimated 43–70% of ovarian metastases are bilateral (3). Metastases to the ovary are

associated with aggressive disease and poor outcomes (4). For young women with colon cancer, available treatment options often impact fertility. Even small doses of radiation to the ovary can effectively sterilize premenopausal women, with estimates of just 14.3 Gy inducing complete ovarian failure, and radiation tolerances for the ovary limited to just 2 Gy (5). Ovarian transposition is a surgical approach to limit ovarian radiation exposure and preserve fertility. However, it is contested whether ovarian preservation in

^ ORCID: Shari Bodofsky, 0000-0002-5583-7612; Evita Sadimin, 0000-0003-4275-1358; Matthew P. Deek, 0000-0002-5949-5058.

reproductive age women with colon cancer is advantageous or presents a significant risk for disease recurrence and subsequent morbidity and mortality.

We present a case report of a young female with locally advanced colon cancer who underwent transposition of the contralateral ovary and subsequently experienced metachronous metastasis post chemoradiation and a discussion of the role of ovarian preservation versus prophylactic bilateral oophorectomy. Our case is unique in addressing a premenopausal patient with fertility concerns, for whom the consequences of unnecessary oophorectomy, or of undertreated malignancy, are particularly devastating. We present the following case in accordance with the CARE reporting checklist (available at <https://dx.doi.org/10.21037/jgo-21-558>).

Case presentation

A 29-year-old female with past medical history of hydronephrosis and insertion of left ureteral stent for nephrolithiasis presented with large bowel obstruction. Flexible sigmoidoscopy revealed a partially obstructing tumor in the sigmoid colon with adenomatous glandular epithelium and high-grade dysplasia. A 5 mm right lower lung nodule was found on computerized tomography (CT) scan of the chest, but otherwise no evidence of metastatic disease was present in scans of the abdomen or pelvis. At the time of her hospitalization, her level of carcinoembryonic antigen (CEA) was elevated at 24.1 ng/mL and both cancer antigens 19-9 and 125 were within normal limits.

She subsequently underwent upfront low anterior resection in addition to ureterolysis and left salpingo-oophorectomy due to direct extension of the tumor into the left ureter. Pathology revealed invasive adenocarcinoma of the sigmoid colon, with 3 positive lymph nodes, and negative resection margins resulting in stage pT4bN1b disease. Adjuvant 5-FU, oxaliplatin, and leucovorin (FOLFOX) chemotherapy was administered for 10 cycles. Five months postoperatively, her CEA level had decreased to 1.1 ng/mL. At this time, additional chemoradiation was recommended to improve local control and prevent recurrence. Due to fertility concerns, the gravida 2, para 1 patient underwent interval transposition of the right ovary into the right lower quadrant and right salpingectomy. Afterwards, the patient received 3-D conformal radiation therapy to the rectum with parameters of 4,500 cGy in 25

fractions with concurrent 825 mg/m² capecitabine taken twice daily for 5 days per week.

One month after completion of chemoradiation, and 10 months since initial diagnosis, the patient presented to the emergency department (ED) with abdominal pain, with CT scans showing possible ovarian torsion. Restaging CT scans completed one month after her ED stay revealed an enlarged, cystic right ovary with ovarian torsion excluded by ultrasound (*Figure 1*). At that time, CEA levels also began to trend upwards, reaching a peak of 68.4 ng/mL two months after completion of chemoradiation. Diagnostic laparoscopy, at this point 1 year after initial diagnosis of colon cancer, revealed right ovarian metastasis with no evidence of peritoneal metastases. Right oophorectomy successfully cleared the ovarian mass. The ovary measured 8.0×6.5×6.3 cm³ and weighed 240 grams. Tumor replaced almost the entire ovarian parenchyma and grossly appeared multicystic, with friable to solid, tan-white to tan-yellow, nodules occupying the majority of the cystic spaces. On histology, the tumor was entirely composed of large glands with garland-like pattern, extensive luminal necrosis and occasional calcifications, consistent with metastatic adenocarcinoma from colonic origin (*Figure 2*). A panel of immunohistochemistry further supports the diagnosis.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). 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 editorial office of this journal.

Discussion

We present a case of a 29-year-old female who underwent ovarian transposition of the right ovary as a fertility sparing measure before initiating radiation for primary left-sided colon adenocarcinoma. Months later, she was diagnosed with a right ovarian metastasis requiring right oophorectomy. For this patient, and for others facing critical decisions about ovarian preservation in advanced colorectal cancer, the question remains how to balance fertility concerns with optimal minimization of metastasis and recurrence (*Table 1*). There is no clear consensus on when ovarian preservation is permissible, especially in the

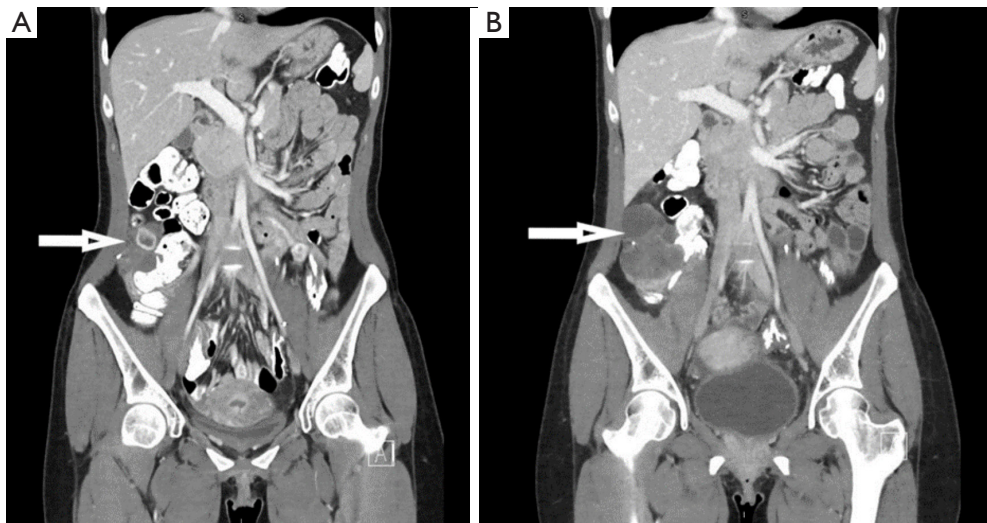


Figure 1 Metastatic progression in the transposed ovary of a 29-year-old female with colorectal adenocarcinoma primary. CT scans of the abdomen and pelvis, 2 months progression. (A) Status post left oophorectomy, post interval transposition of the right ovary into the right lower quadrant with adjacent surgical clips. The ovary is situated between the anterior abdominal wall and the ascending colon. The right ovary appears enlarged, measuring 5.2×2.5 cm², previously normal in size. (B) The right ovary is enlarged, measuring 7.9×3.9 cm², and contains multiple cysts. Differential included ovarian torsion and metastasis. Subsequent oophorectomy and pathological analysis confirmed metastasis. CT, computerized tomography.

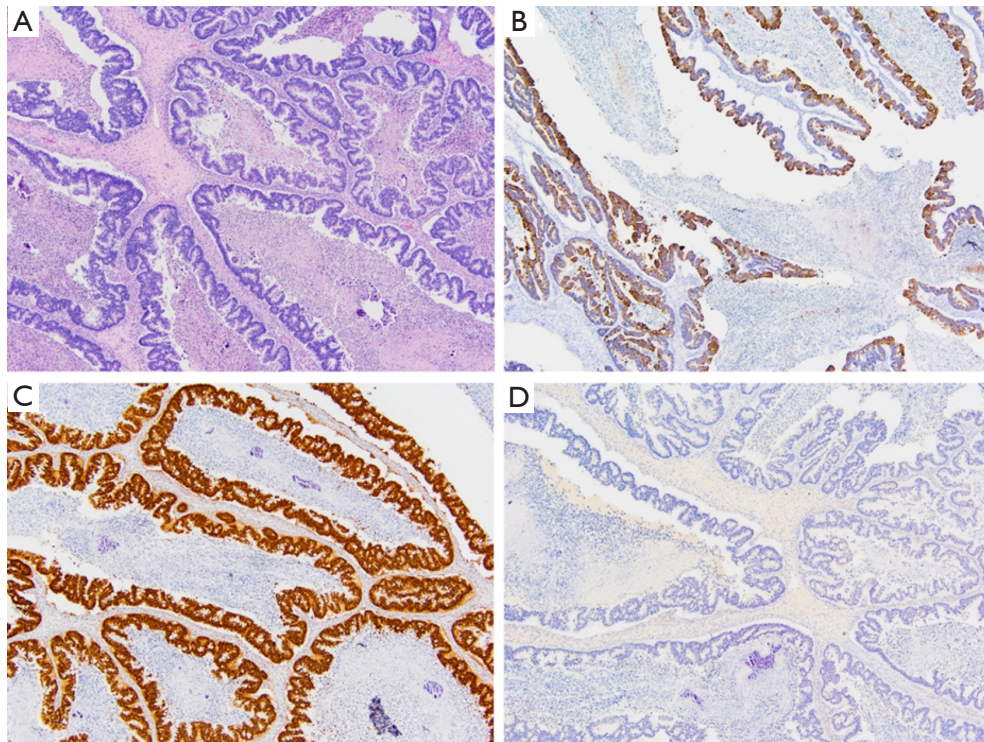


Figure 2 Tumor Histology in a 29-year-old female with metachronous ovarian metastasis. Pictomicrographs of an ovarian tumor in a 29-year-old female with metachronous metastasis after undergoing low anterior resection, left oophorectomy, and right ovarian transposition for colon adenocarcinoma. The tumor is composed of large glands with extensive necrosis and occasional calcifications (A). By immunohistochemistry, it is positive for CK20 (B), CDX2 (C), while negative for PAX8 (D) and CK7 (not shown). All images are shown under 40 \times magnifications.

Table 1 Support for ovarian preservation via transposition versus prophylactic oophorectomy in premenopausal colorectal cancer patients

Ovarian preservation	Prophylactic oophorectomy
Equal survival outcomes Increased overall survival has not been demonstrated in premenopausal patients with CRC who underwent prophylactic oophorectomy	Addresses microscopic disease If peritoneal involvement is present and one ovary presents with metastases, there is a 45% chance the remaining ovary harbors microscopic disease (6)
Avoids hormonal complications Avoids low estrogen levels which are associated with cardiac, bone loss, and neurological complications; may require hormone replacement therapy (7)	Eliminates high incidence of recurrence in remaining ovary If only the affected ovary is removed at initial surgery, 4 out of 5 patients recurred in the remaining ovary (4)
Prevents sterilization Patients avoid sterilization and expensive fertility interventions (egg donors, IVF) if future pregnancies are desired	Prevents reoperation Declining status may prohibit additional operations when recurrence is discovered (8)
Minimizes psychological impact Allows patients to focus on CRC management and associated treatment and lifestyle changes, avoids additional sense of loss	Avoids involvement in new anatomic regions By relocating the ovary into a new anatomic location, previously uninvolved structures face heightened risk of involvement should recurrence develop in the transposed ovary

premenopausal population.

Review of the available literature has shown metastasis to the ovary is present in 0.8–7.4% of colorectal cancer cases (2). The route of spread from the large bowel to the ovary is not definitively known, but may include transcoelomic spread, hematogenous metastasis, lymphatic spread, and direct extension (*Figure 3*). While our patient presented with direct tumor extension into the left ovary at initial surgery, it is less clear the mode of metastasis responsible for the metachronous metastasis to the right ovary. As summarized in Hanna and Cohen, metachronous metastasis to the ovary is uncommon, occurring in 1.4–6.8% of colorectal cancer cases, and usually occurs within 2 years of primary resection (2). Ovarian metastasis is more common in premenopausal patients, which may be associated with their stronger vascular supply, creating a “sanctuary” for metastasis.

For patients like ours, who initially present with synchronous ipsilateral metastasis, the question of how to best address the contralateral ovary remains. Retrospective data in patients with CRC with peritoneal involvement suggests that if one ovary is involved, there is a 45% chance that the second ovary will have microscopic involvement (6).

However, it is unclear whether this data can be extrapolated to our patient, who did not exhibit peritoneal involvement. In one study, of the five patients who presented with synchronous ovarian metastasis and underwent removal of only the affected ovary, four experienced recurrences in the remaining ovary (4). Additional case reports have pointed to the seriousness of metastasis to the remaining ovary, highlighting that the patient’s condition may not permit additional operations (8). Morbidity and mortality are greatly increased for patients with ovarian metastasis compared to those without, with a median survival of just 20 months (9). For this reason, there is considerable interest in preventing ovarian metastasis when feasible.

While initially it may seem that prophylactic bilateral oophorectomy would be advisable, there is considerably disagreement regarding its role, particularly in premenopausal patients. Notably, increased overall survival due to prophylactic bilateral oophorectomy has only been demonstrated in postmenopausal women (10,11). Proposed advantages include potential removal of microscopic synchronous metastases, reduction of metachronous metastases, and eliminating the need for repeated or emergent operation (2). No conclusions have been drawn

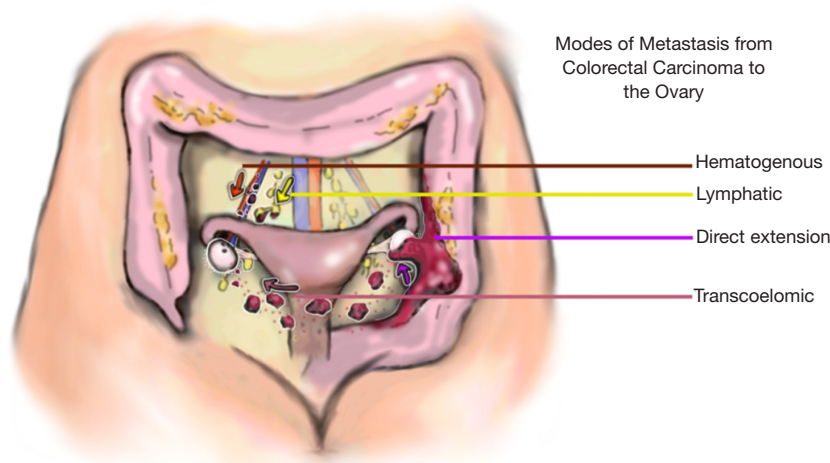


Figure 3 Modes of metastasis from colorectal carcinoma to the ovary. Illustration of the modes of metastasis from colorectal carcinoma to the ovary. Proposed modes of metastasis include hematogenous spread via the blood, lymphatic spread via the pelvic lymph nodes, direct extension from the primary tumor into the adjacent ovary, and transcoelomic spread across the peritoneal cavity.

on its benefit in premenopausal patients. However, bilateral prophylactic oophorectomy comes with risk of significant morbidity and potential development of cardiac, bone, and neurological complications if patients do not receive estrogen replacement therapy (7). Oophorectomy may also cause significant psychological stress and necessitate invasive and expensive fertility treatment.

Thus, the use of prophylactic bilateral oophorectomy in premenopausal women requires careful and individualized consideration. Facing a lack of evidence for survival benefit, hormonal complications, and sterilization, some choose not to pursue prophylactic oophorectomy. However, their fertility concerns often extend to the medical and radiation therapies used to control their primary malignancy. Radiation therapy can effectively sterilize women in their 30 s, with estimates of 14.3 Gy inducing ovarian failure and the threshold for ovarian preservation is limited at just 2 Gy (5). These patients may undergo ovarian transposition, a surgical procedure to relocate the ovary while maintaining its native blood supply, removing it from the radiation field, and preserving reproductive potential. For patients such as ours, with involvement at one ovary, and the intention

of future pregnancies, the decision to undergo ovarian transposition of the remaining ovary is largely dictated by personal choice, as little data instructs an obvious clinical decision. However, our patient now faces disruptive clinical symptoms and reoperation as well as the risk of reducing survival outcomes. There is additional concern that transposition of an ovary harboring microscopic disease may effectively spread the disease to new sites in the abdomen or peritoneum.

While it is difficult to make any firm conclusions on the treatment of similar cases, it is important to note the growing body of case reports pointing to metastasis and poor outcomes in patients who chose not to undergo prophylactic bilateral oophorectomy (*Table 2*). Our case addresses a premenopausal patient with fertility concerns, for whom the consequences of unnecessary oophorectomy, or of undertreated malignancy, are particularly devastating. The case is unique in presenting recurrence in a transposed ovary. Providing informed, scientifically guided medical advice to such patients will depend on future studies investigating the outcomes of prophylactic surgical intervention before chemoradiation.

Table 2 Case reports of metastasis to the ovary postoperatively in colorectal adenocarcinoma

Preoperative diagnosis	Primary operation	Menstruation status	Outcome	Reference
Mucinous adenocarcinoma of appendix, right colon adenocarcinoma	Right hemicolectomy	Premenopausal	Left ovarian metastasis, widespread disseminated disease and death	(12)
Rectal carcinoma	Anterior resection	Premenopausal	Right ovarian metastasis at 16 months, left ovarian metastasis at 31 months, death at 36 months	(8)
Rectal carcinoma with left ovarian metastasis and peritoneal involvement	Anterior resection and left salpingo-oophorectomy	Premenopausal	Right ovarian metastasis at 16 months, death at 32 months	(8)
T3N1M0 colon adenocarcinoma	Right hemicolectomy	Premenopausal	Bilateral ovarian metastasis at 23 months	(13)
Transverse colon carcinoma	Transverse colectomy	Premenopausal	Left ovarian metastasis at 1.5 years, death at 5 years	(14)
Cecal adenocarcinoma with right ovarian metastasis	Right hemicolectomy and right oophorectomy	Postmenopausal	Right ovarian metastasis at 8 years	(15)
Carcinoma of descending colon and simultaneous hepatic metastasis	left hemicolectomy and hepatectomy	Postmenopausal	Ovarian metastasis at 1 year post chemotherapy	(16)
Ascending colon carcinoma	Right hemicolectomy	Postmenopausal	Right ovarian metastasis at 7 months, left ovarian metastasis at 58 months	(8)
T3N0M0 adenocarcinoma of sigmoid colon	Left hemicolectomy	Postmenopausal	Right ovarian metastasis at 3 years	(17)

Case reports identified via PubMed search in August 2021, keywords “colorectal metastasis to ovary”, “recurrence ovarian transposition” and “metachronous ovarian metastasis” with case report filter, selected for relevance.

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Footnote

Reporting Checklist: The authors have completed the CARE checklist. Available at <https://dx.doi.org/10.21037/jgo-21-558>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://dx.doi.org/10.21037/jgo-21-558>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures

performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). 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 editorial office of this journal.

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