CLINICAL VIGNETTE

Neoadjuvant Chemotherapy in Newly Diagnosed Ovarian Cancer

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Introduction

In 2021, it is estimated that 21,410 women will be diagnosed with ovarian cancer and 13,770 with die of their disease. The incidence of ovarian cancer increases with age with the median age at diagnosis, 63-years-old.[1] The most common subtype of ovarian cancer is epithelial ovarian carcinoma (EOC) which accounts for 85 to 90 percent of ovarian cancers.[2] EOC commonly spreads to the lining and organs of the pelvis and abdomen first before spreading to other parts of the body, such as the lungs and liver, and commonly presents with nonspecific symptoms. Treatment includes surgical resection and chemotherapy. If primary debulking surgery is not feasible, then neoadjuvant chemotherapy (NACT) can be administered.

Presentation

A 62-year-old female with a past medical history of chronic constipation, hypothyroidism, and diabetes presented to oncology clinic for evaluation of newly diagnosed ovarian cancer. She initially presented to her primary care physician with worsening constipation. She was referred to gastroenterology who recommended a colonoscopy. The initial procedure was aborted due to poor prep. The rescheduled colonoscopy revealed a submucosal rectal lesion and a significantly narrowed rectosigmoid colon consistent with external compression. CT abdomen/pelvis showed rectosigmoid thickening, bilateral enlarged ovarian masses, extensive peritoneal carcinomatosis, ascites, and bilateral hydronephrosis. CT chest showed multiple enlarged mediastinal lymph nodes and a right pleural effusion. Biopsy confirmed high-grade serous carcinoma, consistent with mullerian primary. CA-125 was elevated at 1200.

She was referred to medical oncology and surgical gynecologic oncology. She was treated with three cycles of neoadjuvant chemotherapy with carboplatin, paclitaxel, and bevacizumab. Repeat imaging showed decreased size in bilateral adnexal masses and improvement in peritoneal carcinomatosis, ascites, and right pleural effusion. Repeat CA-125 was 20. She underwent optimal cytoreduction with total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendectomy, and tumor debulking of implants followed by three cycles of adjuvant chemotherapy with carboplatin, paclitaxel, and bevacizumab. Pathology confirmed high-grade serous carcinoma with moderate treatment effect.

Discussion

Ovarian cancer is the second most common gynecologic malignancy and the most common cause of gynecologic cancer death in the United States.[3] Presenting symptoms are often nonspecific and include pelvic pain or pressure, bloating, urinary urgency or frequency, and gastrointestinal symptoms. As such, most women are diagnosed with advanced stage disease.

For most women, ovarian cancer is treated with primary cytoreductive surgery (PCS) followed by adjuvant chemotherapy. The best outcomes have been observed in women who achieve complete resection of all visible disease.[4] However, neoadjuvant chemotherapy followed by interval cytoreductive surgery is considered for patients with advanced-stage ovarian carcinoma who are not ideal candidates for primary cytoreductive surgery due to poor performance status, comorbidities, or disease unlikely to be optimally cytoreduced.[5] The goal of neoadjuvant chemotherapy is to reduce perioperative morbidity and mortality and increase the likelihood of complete resection of the disease.

Available data suggests overall survival (OS) for selected women with advanced stage ovarian cancer who undergo neoadjuvant chemotherapy followed by interval cytoreduction and adjuvant chemotherapy is similar to women who undergo primary cytoreduction followed by adjuvant chemotherapy.[6,7] Moreover, neoadjuvant chemotherapy is associated with less perioperative morbidity and mortality including fewer bowel resections, ostomies, and post-operative complications.

Several randomized trials have compared neoadjuvant chemotherapy followed by interval cytoreductive surgery to upfront surgical cytoreduction in women with advanced stage ovarian cancer that were unlikely to achieve optimal cytoreduction with upfront surgery. In EORTC 55971, primary cytoreductive surgery followed by 6 cycles of platinum-based chemotherapy was compared to 3 cycles of platinum-based neoadjuvant chemotherapy followed by interval cytoreduction and then at least 3 cycles of adjuvant chemotherapy in 670 women with advanced stage ovarian cancer.[6] Optimal cytoreduction (ie residual tumor <1cm) was achieved in 41.6% of women in the primary cytoreduction arm compared to 80.6% in the neoadjuvant chemotherapy arm. Outcomes were noninferior with overall survival 30 months in the NACT arm vs 29 months in the PCS arm. Perioperative morbidity and mortality were lower in the NACT arm. The CHORUS clinical trial compared

primary cytoreductive surgery followed by 6 cycles of platinum-based chemotherapy to 3 cycles of platinum-based neoadjuvant chemotherapy followed by interval cytoreduction and then 3 cycles of adjuvant chemotherapy in 550 women with Stage III and IV ovarian cancer.[7] Optimal cytoreduction was achieved in 41% of women in the PCS arm and 73% in the NACT arm. Again, the NACT arm was found to be noninferior to the PCS arm with OS 24.1 months vs 22.6 months, respectively. Further, perioperative adverse events were less common in the NACT arm.

Although, neoadjuvant chemotherapy was associated with improved surgical outcomes, it has not been associated with significant difference in overall survival. This may be related to selection of higher risk patients and low rates of optimal cytoreduction in the above clinical trials.

Neoadjuvant chemotherapy should be considered for patients with advanced-stage ovarian carcinoma who are not good candidates for primary cytoreductive surgery or have a low likelihood of achieving optimal cytoreduction with upfront surgery. Outcomes comparable to upfront cytoreductive surgery with less perioperative morbidity and mortality.

REFERENCES

1. Key Statistics for Ovarian Cancer. American Cancer Society. Updated January 12, 2021. Accessed August 2021. https://www.cancer.org/cancer/ovarian-cancer/about/key-statistics.html
2. What is Ovarian Cancer. American Cancer Society. Updated April 11, 2018. Accessed August 2021. https://www.cancer.org/cancer/ovarian-cancer/about/what-is-ovarian-cancer.html
3. Cancer Stat Facts: Ovarian Cancer. National Cancer Institute: Surveillance, Epidemiology, and End Results Program. Accessed August 2021. https://seer.cancer.gov/statfacts/html/ovary.html
4. **Winter WE 3rd, Maxwell GL, Tian C, Carlson JW, Ozols RF, Rose PG, Markman M, Armstrong DK, Muggia F, McGuire WP; Gynecologic Oncology Group Study**. Prognostic factors for stage III epithelial ovarian cancer: a Gynecologic Oncology Group Study. *J Clin Oncol*. 2007 Aug 20;25(24):3621-7. doi: 10.1200/JCO.2006.10.2517. PMID: 17704411.
5. **Wright AA, Bohlke K, Armstrong DK, Bookman MA, Cliby WA, Coleman RL, Dizon DS, Kash JJ, Meyer LA, Moore KN, Olawaiye AB, Oldham J, Salani R, Sparacio D, Tew WP, Vergote I, Edelson MI**. Neoadjuvant Chemotherapy for Newly Diagnosed, Advanced Ovarian Cancer: Society of Gynecologic Oncology and American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol*. 2016 Oct 1;34(28):3460-73. doi: 10.1200/JCO.2016.68.6907. Epub 2016 Aug 8. PMID: 27502591; PMCID: PMC5512594.
6. **Vergote I, Tropé CG, Amant F, Kristensen GB, Ehlen T, Johnson N, Verheijen RH, van der Burg ME, Lacave AJ, Panici PB, Kenter GG, Casado A, Mendiola C, Coens C, Verleye L, Stuart GC, Pecorelli S, Reed NS; European Organization for Research and Treatment of Cancer-Gynaecological Cancer Group; NCIC Clinical Trials Group**. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *N Engl J Med*. 2010 Sep 2;363(10):943-53. doi: 10.1056/NEJMoa0908806. PMID: 20818904.
7. **Kehoe S, Hook J, Nankivell M, Jayson GC, Kitchener H, Lopes T, Luesley D, Perren T, Bannoo S, Mascarenhas M, Dobbs S, Essapen S, Twigg J, Herod J, McCluggage G, Parmar M, Swart AM**. Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial. *Lancet*. 2015 Jul 18;386(9990):249-57. doi: 10.1016/S0140-6736(14)62223-6. Epub 2015 May 19. PMID: 26002111.