

Systemic Treatment of Stage IV Epithelial Ovarian Cancer; A Case Report

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ABSTRACT

Epithelial ovarian cancer is most common gynecologic malignancy in Pakistan. Primary cytoreductive surgery followed by adjuvant chemotherapy is current standard of care for most of the patients with epithelial ovarian cancer, however neoadjuvant chemotherapy followed by surgery is acceptable alternate option for patients presenting with inoperable advanced disease initially. For most of the stage IV ovarian cancer patients, systemic chemotherapy is mainstay of treatment, but other approaches have been emerged for advanced disease including targeted agents, hormonal therapy and PARP inhibitors.

Keywords: Epithelial Ovarian Cancer, Cytoreductive surgery, Adjuvant Chemotherapy, Mets

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INTRODUCTION

Epithelial ovarian cancer is leading cause of gynecologic cancer mortality. In Pakistan, Epithelial ovarian cancer is the leading gynecologic malignancy and 4th most common malignancy in woman¹. The median age at diagnosis for sporadic disease is approximately 60 years. This cancer is usually asymptomatic until it spreads to upper abdomen & usually presents in stage III or IV. Increasing age, nulliparity, early menarche, late menopause and family history are some common risk factors for this cancer. Common prognostic factors are stage, grade, histologic subtype, volume of residual disease after surgery. Primary cytoreductive surgery followed by systemic adjuvant chemotherapy is current standard of care for epithelial ovarian cancers^{2,3}. For patients with extensive omental and peritoneal disease, ascites and abdominal lymphadenopathy, neoadjuvant chemotherapy followed by debulking / cytoreductive surgery is acceptable and more feasible alternative approach^{4,5}

CASE REPORT

I present here a case of 58 years old female who presented in 2014 with symptoms of abdominal discomfort and hypochondrial pain. Ultrasound abdomen & pelvis showed bilateral pelvic/adnexal masses & liver Mets. On contrast enhanced CT scan (CECT) abdomen pelvis there were multiple liver & spleen Mets, bilateral adnexal masses, abdominal lymphadenopathy & peritoneal deposits. Initial CA-125 was > 1000 ng/ml. Ultrasound guided biopsy from pelvic mass showed high grade serious carcinoma. She was started on CAP (Cisplatin, Adriamycin &

Cyclophosphamide) chemotherapy protocol 3 weekly. CECT after 6 cycles showed complete resolution of liver & spleen Mets and abdominal lymph nodes while reduction in size of pelvic masses peritoneal nodules. She completed 08 cycles chemotherapy. On follow up CECT after 04 months of completion of chemotherapy, bilateral adnexal masses were reduced and there was no liver, spleen Mets & abdominal lymph nodes. She was then referred for cytoreductive surgery. Total abdominal hysterectomy + bilateral salpingoophorectomy (TAH + BSO) + omentectomy was done and per operative findings were bilateral adnexal masses, omental deposits. Histopathology came out to be high grade serous carcinoma involving bilateral ovaries & omentum. She was put under surveillance. During follow up, liver & spleen Mets with peritoneal deposits reappeared with increased CA-125 (168ng/ml) in June 2016. Chemotherapy with Paclitaxel & Carboplatin- 3 weekly started and after 06 cycles CA-125 normalized & liver, spleen & peritoneal Mets completely regressed. 08 cycles of chemotherapy were completed. In 2017, patient redeveloped pelvic masses, liver, spleen & extensive peritoneal disease and abdominal lymphadenopathy with raised CA-125 (>500ng/ml). Again she was started on chemotherapy Gemcitabine plus Cisplatin in Feb 2018 with growth factor support. After 6 cycles, CT scan showed complete resolution of pelvic masses while liver, spleen & peritoneal disease regressed therefore 8 cycles chemotherapy were completed. In Oct, 2018 disease progressed once again with raised CA 125 (1800ng/ml) and this time chemotherapy Topotecan D1-D4 3 weekly started which after 8 cycles showed partial response on Mets & lymph nodes. Patient was planned for antiangiogenic drug Bevacizumab but not started due to financial constraints, so she started with single agent

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carboplatin, and after 4 cycles CA-125 dropped to 66ng/ml but treatment interrupted and delayed multiple times due to severe thrombocytopenia, however she completed 8 cycles of carboplatin. Post chemotherapy CECT showed disease progression. Now, hormonal therapy Letrozole has been started to her. Patient is still in good performance status even after 6 years of Metastatic cancer.

DISCUSSION

Primary cytoreduction (optimal cytoreduction defined as less than 1cm residual disease after surgery) followed by systemic chemotherapy is currently standard of care in management of early & locally advanced Epithelial ovarian cancer^{2,3}. Potential advantages of initial surgical management include assessment of disease (staging) histologic confirmation of type and grade, benefit of maximal debulking preceding chemotherapy. For patients who present with inoperable, extensive disease neoadjuvant chemotherapy offers benefit of down staging disease to make surgery feasible & Optimally cytoreducible^{4,5}.

Platinum based chemotherapy is a backbone of Adjuvant/Neoadjuvant systemic chemotherapy. Different acceptable protocols which are used, based on different toxicity profile & affordability of patients are Paclitaxel plus carboplatin, Docetaxel plus Carboplatin, Carboplatin plus Liposomal doxorubicin, Cisplatin plus Doxorubicin plus Cyclophosphamide⁶. Ovarian cancers are mostly chemo sensitive but relapses for advanced cancers are common after initial responses. Patients who relapse after 6 months of completion of chemotherapy are termed as platinum-sensitive⁷ and are re-challenged with same protocols but relapses within 6 months are termed as Platinum-resistant and are treated with second-line drugs⁸ including gemcitabine vinorelbine, Topotecan, Capecitabine etc. Antiangiogenic agents Bevacizumab⁹ has been used with 1st line chemotherapy drugs, as maintenance drug after remission and for relapsed disease with or without chemotherapy. Hormonal drug like tamoxifen, letrozole are also used for maintenance of serous and endometrioid adenocarcinomas¹⁰. Recently PARP (Poly ADP Ribose Polymerase) inhibitors have been approved for ovarian cancer patients with BRCA1 & BRCA2 Mutations for maintenance therapy and for relapsed cases as single agent^{11,12}.

CONCLUSION

Based on patient performance status, financial status, healthcare resources, sequential use of different systemic drugs like chemotherapy, antiangiogenic agents, PARP inhibitors and hormonal agents in stage IV ovarian cancer patients can lead to improved survival and good quality of life.

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