Case Report

Breaking the Survival Barriers: A Case of Stage IV Carcinoma Ovary with Brain Metastasis

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Abstract

The case report ascribed a patient of Stage IV carcinoma ovary papillary serous cell carcinoma, who has survived this disease for past 8 years. The patient was treated with neoadjuvant chemotherapy and cytoreductive surgery followed by adjuvant chemotherapy. The patient remained disease free for 1 year thereafter, developed biochemical relapse.. However, for past 8 years, the patient never achieved a complete remission and despite developing progressive disease, responded substantially to the treatment given and is leading her normal life with minimal imperilment. The patient's long-term survival may be attributed to the favorable responses to the treatment received. The management of ovarian cancer is most impressive when tailored to the individual needs of the patient, maximizing its virtue and prolonging the patient's survival rate. The present case may permit pragmatic acumen into the clinical management of Stage IV ovarian cancer.

Keywords: *Chemotherapy, cytoreductive surgery, papillary serous cell carcinoma*

Introduction

Ovarian carcinoma has the second highest incidence rate and is the fifth leading cause of cancer death in women.[1] The average lifetime risk is 1 in 70, with a median age at diagnosis of 63 years. It encamps a wide array of benign and malignant tumors with diverse histologic cell types, clinical features, and survival outcomes. The primary malignant tumors of the ovary include epithelial ovarian cancers, germ cell tumors, and sex cord tumors. Relative to its incidence, epithelial ovarian cancers have substantially high mortality and poor prognosis[2] because of lack of effective screening tools. Only 25% are detected in Stage I at the time of diagnosis. The current therapies for advanced cancer are although improving but have approached a therapeutic plateau. The platinum-based chemotherapy is indicated for patients with high risk or advanced disease. Ovarian neoplasms are highly curable if diagnosed at an early stage, but 75% present with Stage III or IV disease.[2] The 5-year survival rate declines rapidly between Stages I and IV.[3] For Stage III, it is 30%–40% and <10% for Stage IV.[2] Nonetheless, for specific and certain advanced disease patients executing tailored and individualized treatment as per the response of patients, a timely follow-up may accomplish a satisfactory therapeutic outcome. In the present case report, the step-by-step management protocol followed for a patient with Stage IV ovarian cancer who survived for >9 years is illustrated. As it is rare for a patient with advanced-stage ovarian cancer to manifest such favorable prognosis, it is anticipated that the treatment protocol may prove beneficial to clinicians encountering a similar case.

Case Report

A 52 years old female patient presented in March 2012 with chief complaints of abdominal discomfort for past 2 months. The general physical examination was done including per vaginal and per rectal examination. The per vaginal (p/v) examination revealed a nodule of 2 cm × 1 cm in the posterior fornices of the vagina. Biopsy was taken and histopathological examination (HPE) was suggestive of papillary serous carcinoma [Figure 1]. The chest X-ray was normal. Ultrasound abdomen pelvis was done which showed a large solid–cystic mass of 15 cm × 13 cm × 14 cm arising from the pelvis, and it was more toward the right side and reaching up to epigastrium. The features comprising

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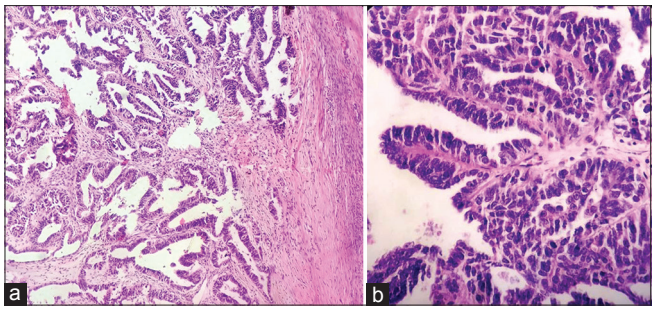

Figure 1: (a) Microscopic examination (low power) shows complex papillary architecture with marked cytological atypia and frequent atypical mitoses suggestive of papillary serous carcinoma ovary. (b) High-power microscopic examination

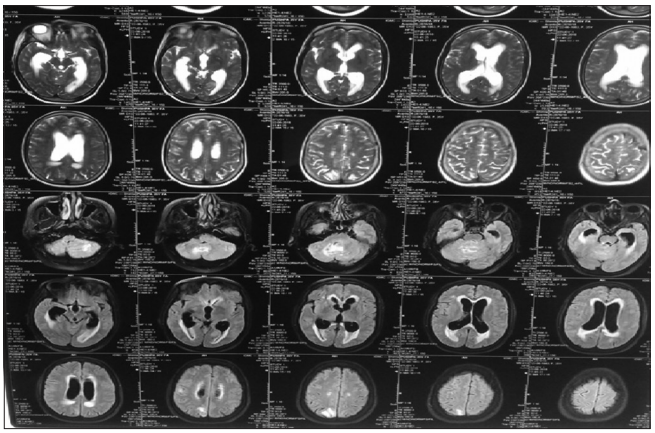

Figure 2: Magnetic resonance imaging brain T2W images and axial and fluid-attenuated inversion recovery images demonstrated multiple well-defined T2 hyperintense lesions seen in the right parietal, left cerebellum, and vermis with surrounding perilesional edema

papillary projections within cystic component and solid component showing vascularity. The bilateral (b/l) ovaries were not demarcated, and the impression was likely to be malignant ovarian tumor. However, the magnetic resonance imaging abdomen and pelvis revealed solid–cystic septate masses measuring 18 cm × 13 cm × 10 cm arising from pelvis with solid component, which was heterogeneous and iso- to hyperintense on T2 and hypointense on T1. The fat planes were lost with uterus, anterior abdominal wall, small bowel, and sigmoid colon. There was evidence of pelvic lymphadenopathy and infiltration into rectovesical and vesicouterine pouch. The liver also showed an altered signal intensity lesion of size 10 mm × 12 mm in segment II. The fine-needle aspiration cytology was also done from this lesion which was suggestive of metastasis. Cancer antigen 125 (CA125) was 5000 U/ml. The patient was staged as carcinoma ovary papillary serous carcinoma Stage IV and started on chemotherapy paclitaxel and carboplatin-based chemotherapy. After four cycles of the chemotherapy, the patient was subjected to exploratory laparotomy with peritoneal sampling with omental biopsy with b/l salpingo-oophorectomy. The detailed HPE was suggestive of serous carcinoma with therapy-associated changes in the left ovary. Right ovary, peritoneum, and omentum were free from tumor invasion. The p/v examination was found to be normal, and CA125 came down to normal limits. Postoperatively, four more cycles of the same chemotherapy were administered, and the patient was kept on 2-monthly follow-up along with serum CA125 levels. After 1 year, the patient had biochemical relapse, positron emission tomography–computed tomography (CT) was also done which showed fluorodeoxyglucose (FDG)-avid subcentimetric serosal deposits in the pelvis, and FDG-avid variable-sized random lung nodules were also noted in b/l lung fields. Hence, the patient was started on second-line chemotherapy, i.e., liposomal doxorubicin, and the patient responded well to the chemotherapy The patient defaulted after receiving four cycles of chemotherapy and presented after 6 months with multiple brain metastases, largest measuring 28 mm × 24 mm size [Figure 2]. Furthermore, contrast-enhanced CT (CECT) thorax depicted multiple nodules in b/l lungs. The patient was started on whole-brain radiotherapy (WBRT) at 30 Gy/10#/2 weeks along with symptomatic treatment. After completion of WBRT after 3 weeks, the patient started on palliative chemotherapy (concurrent chemotherapy [CCT]) based on etoposide and carboplatin and given total six cycles. Biochemical remission occurred, and the patient was asymptomatic afterward and was kept on regular follow-up. The levels of CA125 before and after treatments during the course of the treatment are shown in Chart 1. After 11 months, the patient presented with breathlessness; on CECT thorax suggestive of soft-tissue nodules, b/l lungs increased in size as compared to previous CECT thorax. The patient was rechallenged with paclitaxel- and carboplatin-based CCT; total six cycles were delivered and CA125 levels got normalized. The patient was kept on follow-up for 7 months, again biochemical relapse occurred and CECT showed a metastatic lesion with a further increase in size suggestive of progressive disease. The symptomatic treatment and hormonal therapy were instituted for which the patient also responded well. The last follow-up was done on March 2020, and she was found to be asymptomatic and capable for performing her all daily routine. The step-by-step treatment approach and levels of CA125 are shown in Table 1.

Discussion

Ovarian cancer exhibits the second highest incidence rate and the highest mortality rate among gynecological malignancies.[1,3] About 75% of patients have already reached an advanced stage at the time of diagnosis. Neoadjuvant chemotherapy (NACT) has a controversial role in overall survival rates of patients with ovarian cancer. The European Organization for Research and Treatment of Cancer (EORTC) attained clinical trial results,[4] which supports NACT and validates improvements in survival rates for patients of carcinoma ovary. Nonetheless, the US GOG152 study and a British randomized controlled trial[4,5] demonstrated no benefit in survival rates. Previous joint

Table 1: Treatment given to the patient

Time following diagnosis in months	CA125 level before treatment, U/ml	Treatment	CA125 level following treatment, U/ml
1	5000	Paclitaxel+carboplatin 4 cycles	748
4	748	Interval cytoreductive surgery	19.2
8	19.2	Paclitaxel+carboplatin 4 cycles	6.2
46	155	Liposomal doxorubicin 4 cycles	43
52	904	Treated with WBRT for brain metastasis followed by etoposide and procarbazine six cycles	53
54	111	Symptomatic treatment	237
70	1723	Patient developed secondary lung Re-challenged with paclitaxel+carboplatin six cycles and local RT	40
84	102	Oral hormonal therapy & symptomatic treatment	100
94	100		914
100	800		456

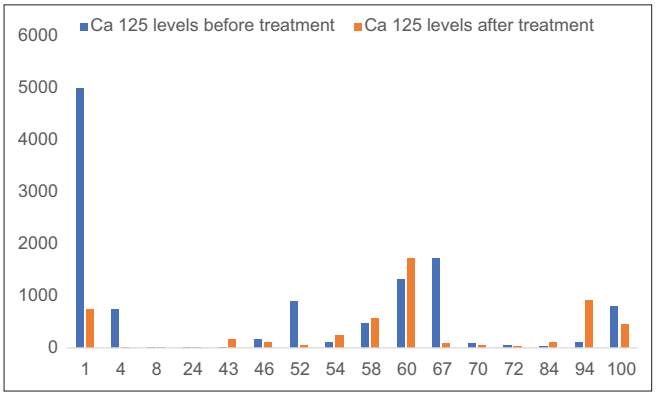

Chart 1: Levels of CA125 prior to and following treatment. CA125: cancer antigen 125

study efforts of the EORTC and National Cancer Institute of Canada identified that NACT is no less effective than standard first-line treatment.[6,7] In the present case, NACT resulted in a favorable outcome. The patient responded exquisitely to NACT. The metastatic lesions disappeared following four cycles of NACT. The patient's general condition improved significantly, which made interval cytoreductive surgery possible. An additional four courses of postoperative chemotherapy achieved complete clinical remission. Although relapse occurred 24 months after surgery, the disease was sensitive to platinum-based chemotherapy with a favorable prognosis. At this stage, the patient was considered for platinum-sensitive chemotherapy for recurrent cancer, where four cycles of combined liposomal doxorubicin second-line chemotherapy were administered. Once again, the disease was effectively controlled. Subsequently, the disease relapsed on multiple occasions and began developing resistance to chemotherapy. However, the patient's disease was controlled effectively for a long time with appropriate modifications to the drug regimen. Eventually, the patient capitulates 8 years after the primary diagnosis. A similar kind of case was reported by Huang *et al*.,[8] and the patient presented with Stage IV disease and offered multiple lines of chemotherapies like in our case. Topotecan, capecitabine, nedaplatin, lobaplatin, and irinotecan were also used in combinations and managed to prolong the survival of up to 9 years. Brain metastasis in ovarian cancer is a subtle and reported in <1% of patients in autopsy cases and in 2% of clinical series. Recent series have suggested an increased incidence as chemotherapy regimens have become more effective.[9] Nonetheless, long-term prognosis is poor, as brain metastases are often a late manifestation of advanced disease, with a median survival time of <12 months. In a series of 24 patients with metastatic brain disease treated with WBRT, stereotactic radiosurgery (SRS), or a combination of WBRT and SRS, the median survival was 8.5 months.[10] Platinum sensitivity was also recently identified as an important prognostic factor in women with metastatic brain involvement from ovarian cancer.

In our case, NACT, interval cytoreductive surgery, and multiple long-term chemotherapies following surgery controlled the disease effectively. Multiple surgeries should not be considered as the standard treatment for recurrent ovarian cancer. Instead, multiple sessions of chemotherapy may be useful in the management of relapsed disease. Moreover, the patient developed lung and brain metastasis, and the reason may be the wide dissemination of disease or may be the nonadherence to the treatment, still the patient managed aggressively and also responded well. So as to conclude, the appropriate and tailored treatment should be selected on the basis of the patient's condition in order to maximize the therapeutic efficacy and survival prolongation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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