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Case of Late Recurrence in Early Stage Epithelial Ovarian Cancer

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ABSTRACT

Epithelial ovarian canceris usually diagnosed in late stage with high recurrence rate and fatality. Long term survival in late recurrence is not very common. We present a case of 66 year woman who had come in early stage of epithelial ovarian cancer. She survived despite having recurrence after 13 years following staging laparotomy with TAH with BSO with infracolic omentectomy and six cycles of adjuvant chemotherapy in 2007. She underwent secondary cytoreduction twice, first in 2013 and second in 2020 after she developed large pelvic mass. First secondary cytoreduction histopathology was inclusion cyst and second time it serous adencarcinoma grade III consistent with the histopathology of 2007. Both times she received chemotherapy after secondary cytoreduction including neoadjuvant chemotherapy (NACT) in 2020. She is doing well on follow up and is on oral etoposide.

Keywords: Chemotherapy; epithelial ovarian cancer; late recurrence; secondary cytoreduction

INTRODUCTION

Epithelial Ovarian Cancer is an aggressive malignancy and frequently diagnosed in advanced stage . In contrast, stage I EOC allows complete surgical excision with favorable prognosis. Surgery for stage I ovarian cancer is primary cytoreduction with retroperitoneal lymph node dissection, and peritoneal biopsy at several sites as part of staging surgery to detect metastasis or dissemination. Controversy regarding systematic lymph node dissection for decreased recurrence. Lymphadenectomy in Ovarian Neoplasms (LION) Study, a phase III RCT examined 657 patients with newly diagnosed stage IIB-IV ovarian cancer who had undergone macroscopic complete resection and had pre- and intraoperatively negative lymph nodes. The authors concluded that systematic pelvic and para-aortic lymphadenectomy in patients with advanced ovarian cancer improved neither overall nor PFS despite detecting (and removing) subclinical retroperitoneal lymph node metastases in 56% of the patients.[1] Prevention of recurrence is important because the outcome after recurrence is poor.

CASE REPORT

A 66 year lady came in 2020 after 7 years of secondary cytoreduction in 2013. In 2013, she was referred to us, as she had developed a mass in the pelvis following staging laparotomy with TAH with BSO with infracolic omentectomy 6 years back in 2007, when she was staged as carcinoma ovary stage 1C. Her histopathology was serous adenocarcinoma of the ovary G III. She received six courses of adjuvant chemotherapy with paclitaxel and cisplatin.

In 2013, she did not have any symptoms but computed tomography (CT) scan showed homogenous well defined mass of 10 x10 cms with no metastasis in other sites and tumor markers as cancer antigen 125 (CA125) and carcinoembryonic antigen (CEA) were within normal limits. With a suspicion of recurrence of ovarian cancer(ROC), she underwent secondary cytoreduction as her performance status was good and the mass looked resectable, confined in the pelvis both clinically and on CT . On laparotomy, the mass was removed without much difficulty as it was not densely adherent to the neighboring organs like bladder and bowel. There was no metastasis in the pelvis and abdomen. The mass was 10x8 cm, smooth, cystic, contained clear fluid and internal surface was smooth. Her histopathology was inclusion cyst and not recurrence or metastasis, so after discussion in tumor board, in view of possibility of pathological proliferation of dormant ovarian cancer cells and microscopic occult dissemination in the intrapelvic peritoneum, and decision was taken to give chemotherapy. She therefore received another 6 cycle of Cisplatin/taxol chemotherapy.

The patient tolerated chemotherapy well and subsequently had no evidence of disease till the first 3 years. There after she did not come for follow up. After 7 years of secondary cytoreduction, she again

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visited us with complaint of urinary frequency for 2 months in 2020. She was obese and on per vaginal examination, there was a firm fixed mass impacted in the pouch of Douglas(POD) and size being difficult to assess. Subsequent CT scan confirmed the presence of a large complex solid cystic abdominopelvic mass with hydronephrosis of right kidney. Chest X ray and CT chest was normal. Serum levels of CA125 and CEA was in normal range. Transabdominal ultrasonography guided aspiration was unsuccessful, so trucut biopsy of mass per vagina done and histopathology report came as clear cell carcinoma. Plan was made to give neoadjuvant chemotherapy (NACT) with paclitaxel and cisplatin as she was Platinum sensitive for six courses . She tolerated the chemotherapy well. However as her findings remained same as before NACT, she underwent secondary cytoreduction for the second time .

On opening the abdomen, it was difficult to find the mass as it was deep in the POD and bowel was adherent all over the mass. (Figure 1) shows the mass after separating the adhesions and (Figure 2) shows the dilated right ureter in between two artery forceps seen penetrating the mass. Complete removal of mass was possible. It was 11x 10 cms, solid in consistency. Figure 3 (A,B) on cut section revealed solid to cystic area with multiple septations. There was no residual mass in the pelvis and abdomen. Liver and undersurface of diaphragm was free of metastasis and there was no palpable lymph nodes. The histopatholgy report came as serous adencarcinoma grade III consistent with the histopathology of 2007 and not clear cell as found in trucut biopsy. The disparity could be a technical problem propably due to large tumor, resulting in necrosis, hemorrhage and degeneration and receiving tissue bits. She was kept on adjuvant oral etoposide by the medical oncologist as she refused for intravenous chemotherapy. After 3 months of surgery, her CT scan revealed no abnormality except for hydronephrosis on right side as prior to cytoreduction.

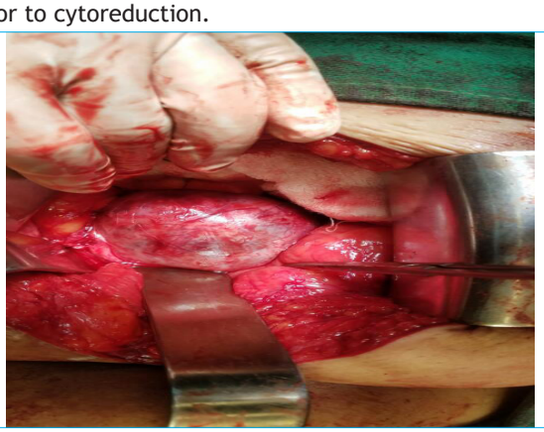

Figure 1. The mass after separating the adhesions.

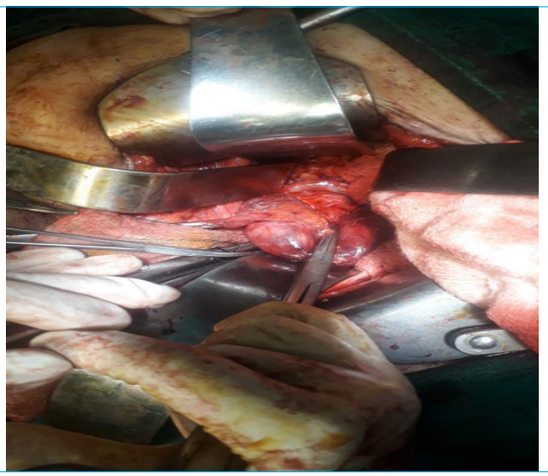

Figure 2. Dilated right ureter inbetween two artery forceps seen penetrating the mass.

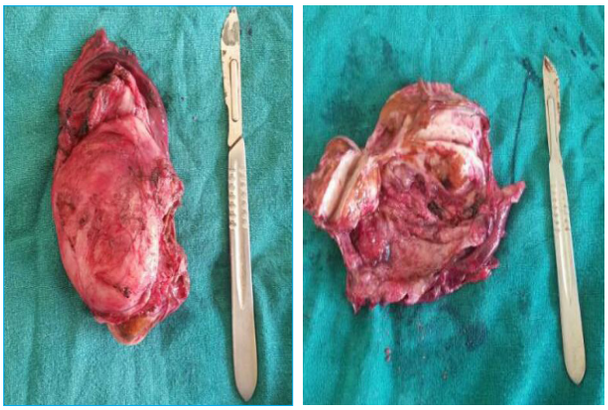

Figure 3. (A,B) Cut section revealed solid to cystic area with multiple septations.

DISCUSSION

She survived despite having recurrence after 13 years. She underwent secondary cytoreduction twice, first in 2013 and second in 2020 after she developed large pelvic mass. She was given paclitaxel and cisplatin as chemotherapy regimens for platinum-sensitive relapsed ovarian cancer which include monotherapy with agents such as cisplatin and carboplatin, as well as combination therapies, including paclitaxel plus carboplatin, carboplatin plus gemcitabine and cisplatin plus gemcitabine.[2,3] The standard approach for treating ROC is chemotherapy, and surgery remains an option for individual patients who should be carefully selected. Patients undergoing surgery showed a prolonged progression free survival (PFS) compared with patients undergoing chemotherapy alone. Surgery was safe as 30, 60 and 90 day mortality was not increased in patients undergoing surgery.[4] Two series describing a benefit of cytoreduction to 1-20 mm compared with >20 mm and 1-10 mm compared with

>10 mm.[5,6]

Several articles have examined the sites of recurrence of stage I ovarian cancer.[7-9] However, details of recurrences sites of stage I EOC have only been reported in 2 studies from multiple institutions in Italy in 1997 and 2013. The first study was a retrospective investigation of 224 FIGO stage I patients, in which recurrence occurred in 39 (17%), including intrapelvic peritoneal recurrence in 54% of recurrence cases.[10] In the second study, recurrence occurred in 87 (19%) of 467 FIGO stage IA-IIA patients, including intrapelvic peritoneal recurrence in 44% of recurrence cases.[11] The high recurrence rate in the peritoneum may partly be due to insufficient investigation of peritoneal lesions at initial surgery. In a study of peritoneal biopsy (6 sites in the pelvis) in the treatment of early-stage ovarian cancer, microscopic disseminated lesions were detected by intrapelvic peritoneal biopsy (4.1%) of 122 patients, and these cases were later upstaged.[12] In another study in which the peritoneum (including the subphrenic peritoneum) was randomly biopsied in 129 patients, no phrenic peritoneal dissemination was found, but microscopic dissemination was present in 7% of cases as lesions of occult dissemination in the intrapelvic peritoneum, and these cases were similarly upstaged.[13] In the National Comprehensive Cancer Network (NCCN) guidelines[14], random peritoneal biopsies should be taken from the pelvis, paracolic gutters, and undersurfaces of the diaphragm . Furthermore, the Gynecologic Oncology Group (GOG) surgical manual recommends peritoneal biopsies from cul-de-sac, vesical peritoneum, right and left pelvic sidewalls, right and left paracolic gutters and right diaphragm for clinical stage I ovarian cancer. These guidelines strongly suggest that patients with occult dissemination in the intrapelvic peritoneum could be included in the cases of stage I EOC, and that routine peritoneal biopsy in the first surgery is necessary. We should do multiple biopsies as advocated by various guidelines as the biological behavior of the EOC is markedly different from the well-studied pattern of hematogenous metastasis found in most other cancers. The progression of metastases onto peritoneal surfaces appears to be very direct for ovarian cancer.[15,16]

Our case had recurrence in the peritoneum. When she was referred in 2007, there was no mention of multiple biopsies of peritoneum, which could have upstaged her. This would have affected her treatment, she would have frequent follow up with imaging studies, nevertheless she remained disease free for several years. Follow up with tumor makers as CA125 and CEA seemed ineffective, as they were normal.

CONCLUSIONS

Recurrence of stage I EOC by peritoneal dissemination is frequent, especially in the pelvis. There is a need to elucidate the pathogenesis of peritoneal recurrence and to prepare treatment strategy to prevent pelvic peritoneal recurrence. For this we have to take multiple biopsies at initial surgery. Patients with recurrent platinum-sensitive ovarian cancer may have increased response rates and longer PFS when treated with combination platinum-based chemotherapy compared to carboplatin alone. Most recurrent patients with platinum resistant disease have little chance for a long PFS, but less toxic treatment may contribute to extending their survival interval. Complete secondary cytoreduction combined with further adjuvant therapy at the time of relapse may improve clinical outcome in selected patients. There are several treatment choices from first relapse to terminal stage, however these choices cannot be made uniformly. They should be decided on an individual basis depending directly on the patients' condition.

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