Changes in the Cancer Antigen Markers in the Pleural Liquid During Chemotherapy among Ovarian Cancer Patients

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Abstract

The silent killer or ovarian cancer (OC) is one of the major causes of cancer deaths among women in the modern age. In view of the therapeutic roles of platinum based chemotherapy among the ovarian cancer patients, objective of this report was to assess the effects of the first round of chemotherapy among women with ovarian cancer. Here, the levels of the pleural markers for cancer bio markers, before and after the chemotherapy were tested among ovarian cancer patients. The biochemical indices may be of use in deciphering the relation between cancer relapse and platinum retrieval. The pleural analyses pre and post platinum chemotherapy session demonstrated wide range of biochemical and protein marker changes among ovarian cancer patients. The various cancer antigens were variedly reduced post chemotherapy. Hence, it is proposed that biochemical markers in pleural liquid may serve as better indicators and early diagnostic tools for ovarian cancer.

Keywords: *Ovarian cancer, chemotherapy, pleural liquid, cancer antigens.*

Introduction

One of the major cancer deaths among women is caused by ovarian cancer (OC). There has been an immense development in the field of cancer therapy, the majority of patients experience disease recurrence and receive second-line and sometimes several lines of treatment [(1-4)]. The progression-free survival among OC patients is fairly constant at about 1.5 years with respect to the modern diagnostic tools and treatment patterns. As high as 80 percent women with advanced stages of OC report tumor progression or recurrence. As high as 70% cases of OC are diagnosed at advanced stages leading to bad prognosis. Generally late-stage ovarian cancer is incurable in the majority of cases. The recent developments in surgical technology and contemporary regimes of systemic treatment, as well as some new drugs have turned the late-stage OC as a chronic condition by extending the survival days [(3)]. The "silent killer" synonym for ovarian cancer is because the majority of patients are diagnosed in late stage, and that in early stages of the disease symptoms are not evident.

Pleural effusion is a common feature among women with OC and breast cancer. Pleural effusion is an abnormal accumulation of fluid in the pleural cavity which is the space between lungs and chest wall [(4)]. The liquid starts accumulating the between the layers of the pleura. When pleural effusion is related to cancer or there are cancer cells in the fluid, it may be called malignant pleural effusion.

Approximately 20% of women with advanced-stage ovarian cancer survive beyond 12 years after treatment and are effectively cured. Initial therapy for ovarian cancer comprises surgery and chemotherapy, and is given with the goal of eradicating as many cancer cells as possible. Indeed, the three phases of therapy are as follows: debulking surgery to remove as much of the cancer as possible, preferably to a state of no visible residual disease; chemotherapy to eradicate any microscopic disease that remains present after surgery; and second-line or maintenance therapy, which is given

to delay disease progression among patients with tumour recurrence [2]. Epithelial ovarian cancer has the highest mortality rate of all gynaecological malignancies. Most women present with advanced disease and develop a recurrence after radical surgery and chemotherapy. Improving the results of first- or subsequent-line chemotherapy has been slow, and novel approaches to systemic treatment are needed. Ovarian cancer is a heterogeneous disease with complex molecular and genetic changes. Understanding these better will provide information on the mechanisms of resistance and opportunities to target therapy more rationally, exploiting specific changes in the tumour [4,5].

Primary debulking surgery followed by platinum-based chemotherapy remains the standard treatment of patients with stage III-IV epithelial ovarian cancer. Neoadjuvant chemotherapy is an alternative treatment regimen that can be considered in selected patients. Complete cytoreduction, both through primary debulking surgery and interval debulking surgery, has a major positive effect on survival and should be the goal, even if this requires extensive surgery. When thorough assessment of tumor spread and performance status of the patient indicates that complete primary cytoreduction is not feasible without unacceptable morbidity, then alternative therapeutic strategies, such as neoadjuvant chemotherapy, must be considered [5,6,7].

Malignant pleural effusion is the most common site of stage IV ovarian cancer. A positive cytology is required for a stage IVA diagnosis. Unfortunately, the accuracy rate of pleural cytology remains low. A number of factors have been identified as prognostic for clinical outcomes in patients with epithelial ovarian cancer [7,8,9]. The pleural cavity constitutes the most frequent extra-abdominal metastatic site in ovarian carcinoma (OC). In patients with OC and pleural effusions, a positive fluid cytology is required for a stage IV diagnosis. Unfortunately, about 30% of malignant pleural effusions exhibit false-negative cytological pleural fluid results. In those circumstances, exploratory video-assisted thoracoscopic surgery (VATS) serves as a diagnostic, staging and even therapeutic modality [8,9].

We hypothesize that the pleural liquid markers could serve as significant markers of disease progression and response to therapy among OC patients before and after one cycle of chemotherapy.

Materials and Methods

Participants: All participants (patients) were enrolled as part of clinical trial going on according to the IP and GCP/GLP guidelines at a reputed hospital. Patient/ immediate relative consents were obtained for using the serum/plasma for research and data management.

Drug and dosage: PEG-ylated liposomal cis-platin is a formulation of cis-platin in polyethyleneglycol-coated liposomes with a prolonged circulation time. Cisplatin intercalates between base pairs in the DNA helix, thereby preventing DNA replication and ultimately inhibiting protein synthesis. Dosage is calculated by estimating Body Surface Area (BSA) and at 50mg/m^2 BSA is infused intravenously (2mg/ml).

$$\mathbf{BSA\ (m2)} = \sqrt{\frac{\text{(height (cm)X weight (kg)}}{3600}}$$

Collection of Pleural liquid: Patients having ovarian cancer were selected by the Medical Practitioner and suggested for the study (n=31). The pleural samples were collected before the initiation of chemotherapy (PEGylated cis-platin liposomes) and after three weeks of first chemotherapy session (PEG= poly ethylene glycol).The Pleural liquid of the patient was collected by the nursing professional and immediately introduced into collection bottles. Approximately 100ml aliquot from each patient was collected and immediately used for all the biomarkers and stored at -20° C.

Estimation of the biomarkers: Level of pleural markers were estimated by using ELISA kits according to manufacturer's instructions.

Statistical Analysis

The data expressed as mean ± SE were analyzed by one-way ANOVA followed by a post hoc Tukey's test to compare the control and treatment groups as well as

among the groups ($p \leq 0.05$) using GraphPad Prism 5.0 software. Different alphabet letters indicate significance difference among the respective groups. In some assays, * indicates significance difference from control ($p \leq 0.05$).

Results and Discussion

Among the ovarian cancer patient volunteers who belonged to an age range of 43 to 65 years, nearly 45% of them complained of pain in the abdominal area while 35% of them presented nausea as their main symptom. In my previous report I demonstrated that the pleural thickening was significantly reduced among the ovarian cancer patients after first round of Platinum-based chemotherapy. The reduction in the pleural thickness is observed in most of the clinical trials. However, in this study, the reduction was not to a marked extent but significant change was recorded. The hexose levels were unaffected while the cholesterol was markedly increased among the patients. Anti-inflammatory markers also elevated among chemotherapy patients which was duly reported in my previous publication. As a proof of principle, the chemotherapy resulted in biochemical changes in the pleural liquid among ovarian cancer patients.

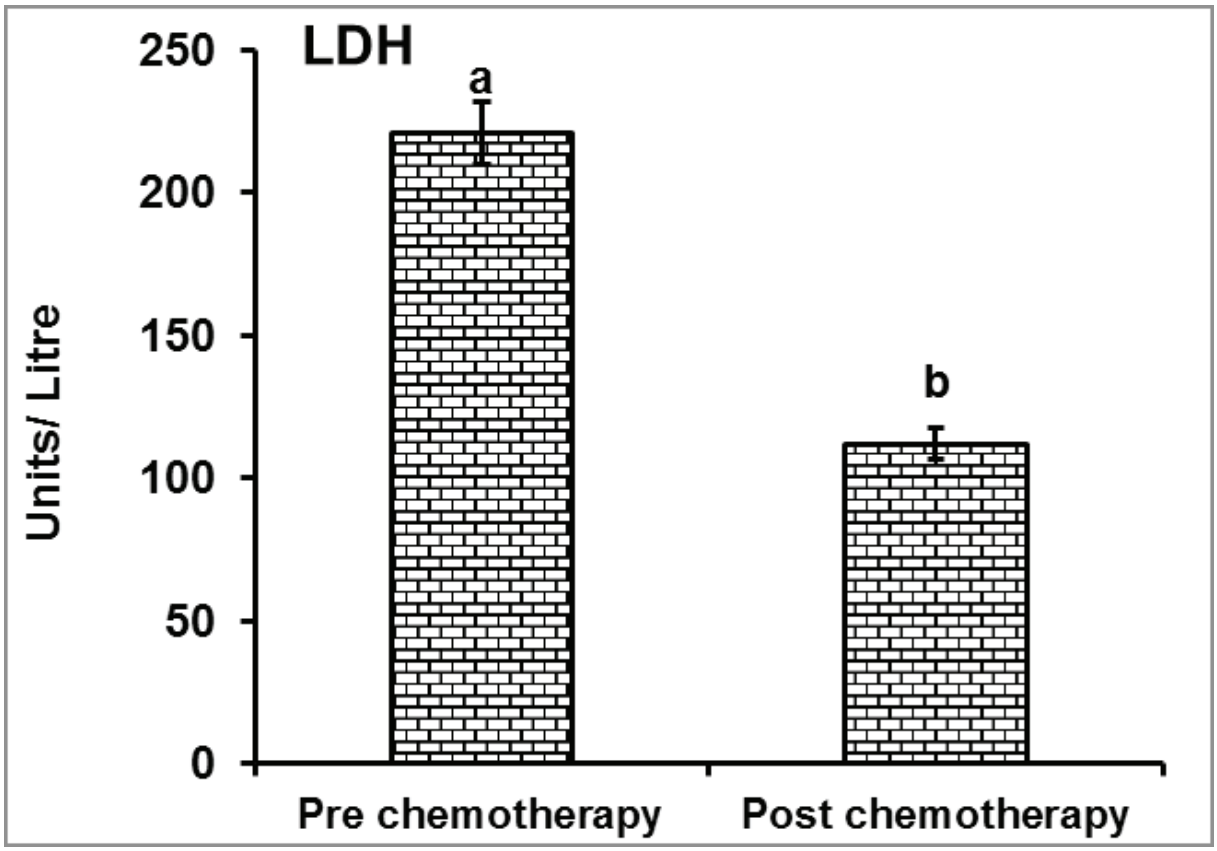

Figure 1. Effect of chemotherapy on the Lactic dehydrogenase activity in the pleural liquid among patients of ovarian cancer before and after one cycle of chemotherapy (n=31). Different letters indicate significant difference between groups ($p \leq 0.05$).

The enzymic levels of Lactic Dehydrogenase were decreased among post chemotherapy samples (Figure 1).

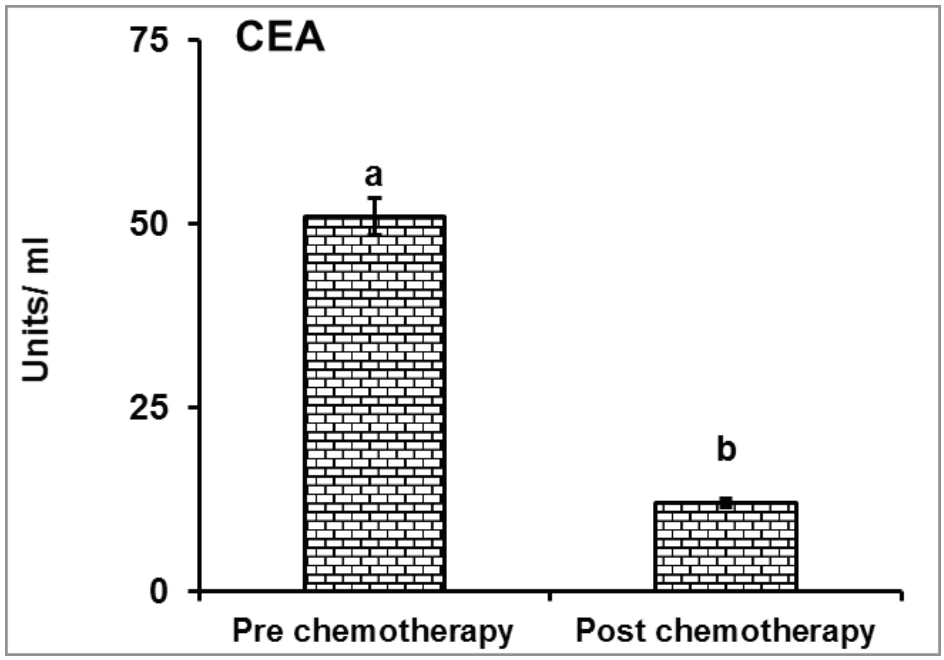

Figure 2. Effect of chemotherapy on the CEA levels in the pleural liquid among patients of ovarian cancer before and after one cycle of chemotherapy (n=31). Different letters indicate significant difference between groups (p≤0.05).

The cancer Biomarker: Carcinoembryonic antigen (CEA) levels were significantly reduced among post chemotherapeutic samples, however, the levels were not reaching the safe diagnosis (Figure 2).

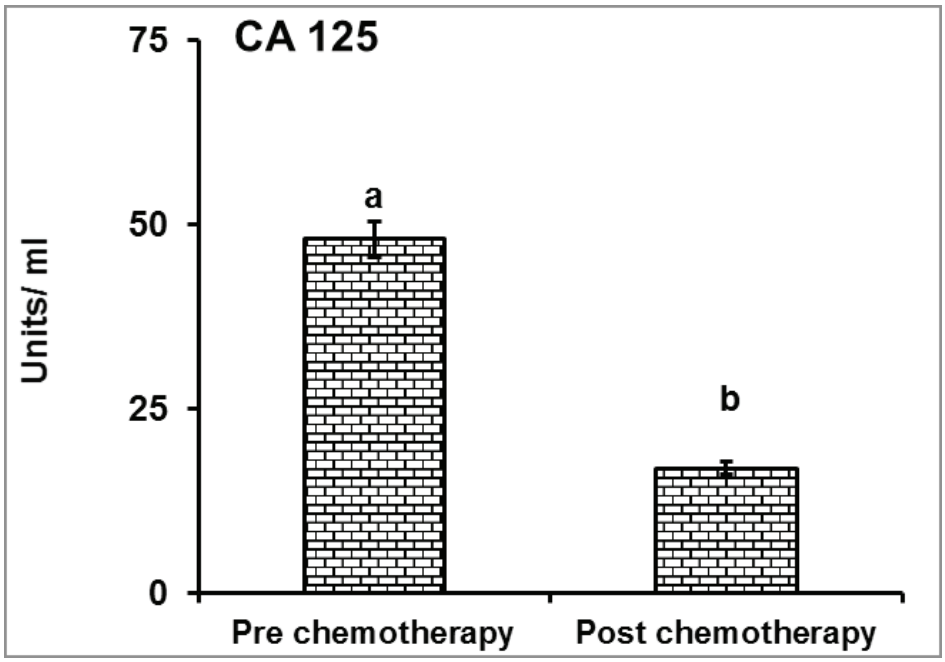

Figure 3. Effect of chemotherapy on the CA 125 in the pleural liquid among patients of ovarian cancer before and after one cycle of chemotherapy (n=31). Different letters indicate significant difference between groups (p≤0.05).

The cancer Biomarker: Cancer antigen (CA 125) levels were significantly reduced among post chemotherapeutic samples (Figure 3). However, the levels were not reaching the safe diagnosis levels.

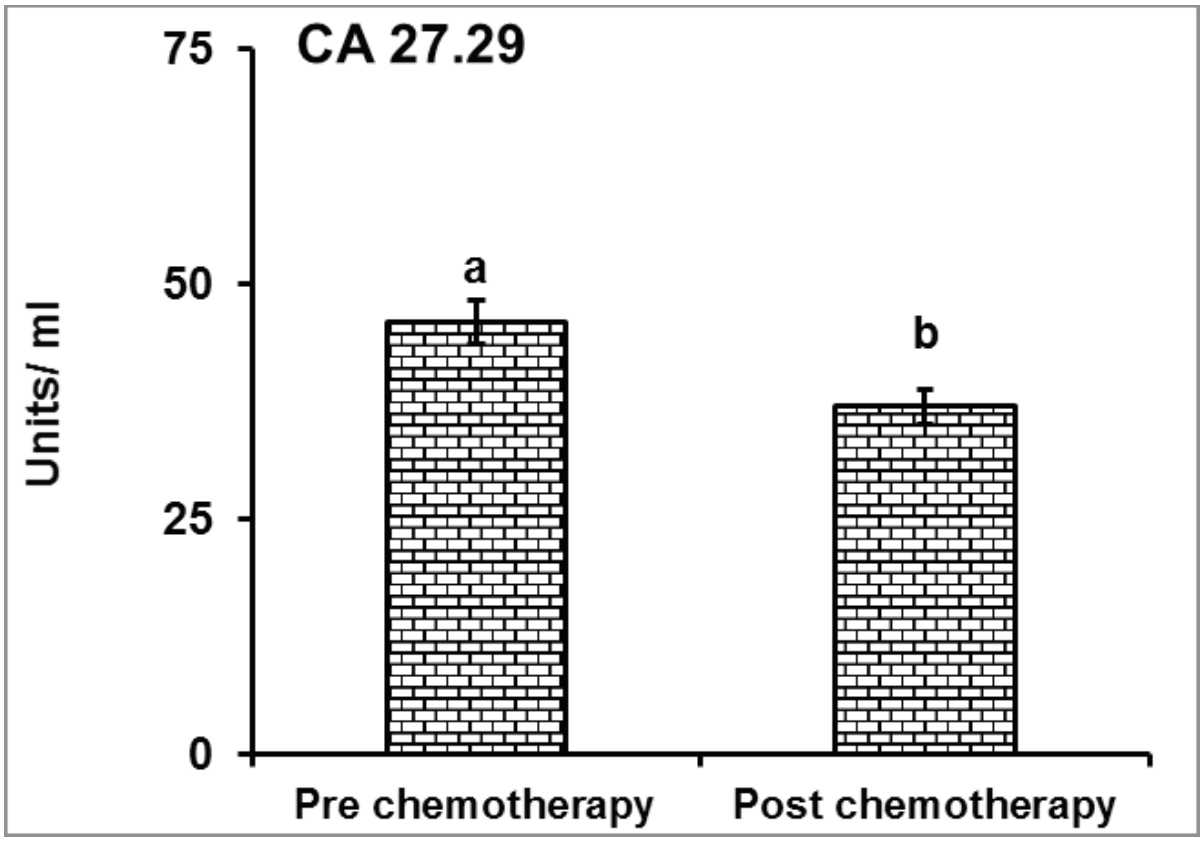

Figure 4. Effect of chemotherapy on the CA 27.29 in the pleural liquid among patients of ovarian cancer before and after one cycle of chemotherapy (n=31). Different letters indicate significant difference between groups ($p \leq 0.05$).

The cancer Biomarker: Cancer antigen (CA 27.29) levels were very marginally but significantly reduced among post chemotherapeutic samples, however, this data is suggestive that multiple sessions of chemotherapy could bring down the cancer marker levels (Figure 4).

Conclusion

Analysis of the pleural samples from ovarian cancer patients before and after one round of chemotherapy revealed that there were varied biochemical changes. In lines with my previous report, here additional data about cancer antigen markers are presented. There was a significant change among cancer antigens in pleural liquid after chemotherapy. Hence, it is proposed that biochemical markers in pleural liquid may serve as better indicators and early diagnostic tools for ovarian cancer.

Conflict of Interest: There are no conflicts of interests.

Acknowledgement: The author thanks the patients who were willing to participate in the study.

Ethical Clearance: This study regimen was approved by and followed the guidelines of the institutional ethical committee.

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