

ORIGINAL ARTICLE

Correlation Between CA-125 and Ovarian Cancer: A Bangladesh Perspective

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Abstract :

CA-125 is an important tumour associated antigen for ovarian cancer in diagnosing and assessing the prognosis of the patient. The rate at which CA-125 levels change is often an indirect measure of the level of cancer growth and inflammation in our body. This paper aims at evaluating the correlation between ovarian cancer, its treatment and CA-125 level. A multicenter prospective study on ovarian malignancy was done. The study team included gynaecologists, oncologists, allistopathologists and an oncology associate from the company (Sanofi-Aventis) supplying the drugs. The patients were enrolled during 1999 to 2002 and have been followed up till now. The level of CA-125 was done from one single identified laboratory for making the result standard. Seventeen patients with different stages and types of ovarian cancer were enrolled in the study. CA-125 level was assessed prior to treatment, at the end of chemotherapy and in the subsequent follow up. Disease status following chemotherapy was also evaluated. When the chemotherapy started, the level of CA-125 started declining in 13 patients and came down to 50% of the previous value at the end of second cycle. The CA-125 level came down to less than 35 U/ml after the end of 3-6 cycles of chemotherapy (normal value is 35 U/ml), and this level came down to less than 10 U/ml in all 13 patients who survived. The decline rate of CA-125 after chemotherapy was 77%. All those patients are found to be clinically disease free and physically well till now. The three year survival rate is 72%. Toxicity profile was also acceptable. CA-125 level is an important investigation for diagnosing ovarian cancer. But the rate of decline of the level of CA-125 following treatment is an important prognostic factor. The chemotherapy used in the study was a combination of Taxotere¹ and Carboplatin.

Introduction :

The ideal tumor marker, which would specifically detect a malignancy and would not be present in nonmalignant tissues, does not currently exist. Most tumor markers are

nonspecific in that they are found in multiple types of malignancies as well as in normal and benign conditions. A number of tumour markers have been studied for ovarian carcinoma, including CA-125. CA-125^{3,4}, the most extensively studied ovarian cancer-associated antigen, is a high molecular weight glycoprotein that is secreted into the blood by ovarian cells⁵. CA-125 levels can provide important insight into the growth of ovarian cancer cells within our body⁶. It has both diagnostic and prognostic value⁷. The rate at which CA-125 levels change is often an indirect measurement of the level of cancer

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growth and inflammation in our body⁸. The CA-125 test only returns a true positive result for about 50% of stage-I ovarian cancer patients². But the test has an 80% chance of returning true positive results from stage-II, III, IV ovarian cancer patients. The other 20% of ovarian cancer patients do not show any increase in CA-125 concentrations. This study has been designed to evaluate the correlation with Taxotere-Carboplatin combination chemotherapy and CA-125 level.

Materials and method :

A multicenter prospective study on chemotherapy for ovarian malignancy has been in progress since 1999. Patients were included from Bangladesh Institute of Research for Diabetes, Endocrine and Metabolism (BIRDEM), Ahsania Mission Cancer Hospital and Holy Family Red Crescent Medical College Hospital. The study team was multidisciplinary and included gynaecologists, oncologists and histopathologists with support from Sanofi-Aventis Oncology. The patients were enrolled during 1999 to 2002 and follow up is being done till now. The level of CA-125 was done from one single laboratory for making the result standard. Seventeen patients at different stages of ovarian cancer, who were histopathologically proven cases of epithelial and germ cell cancer, were enrolled in the study. The age of the patients was between 20 and 75 years. All the patients had raised level of CA-125. Early stage patients were treated surgically and diagnosis was confirmed by biopsy and histopathology. Late stage patients were diagnosed on peritoneal fluid cytology. Among them, fifteen patients (88%) had epithelial cell cancer and two patients (12%) had germ cell cancer. The patients were categorized again on the basis of CA-125 level (normal value is 35 U/ml) into four groups. The groups were as follows: less than 100 U/ml, 100-500 U/ml, 500-1000 U/ml, more than 1000

U/ml. Only one patient had less than 100 U/ml, seven patients had 100-500 U/ml, eight patients had 500-1000 U/ml and one patient had more than 1000 U/ml (3240 U/ml). All patients received 75 mg/m² Taxotere as an one hour infusion and 300 mg/m² Carboplatin, both were given once in every three weeks for a total of 3-6 cycles⁹. CA-125 level was assessed before starting of chemo therapy, at second week of each cycle and after completion of chemotherapy. Further follow up assessment of CA-125 was also done at first monthly for three months and then three monthly till now. Thirteen patients were included in this analysis for evaluation of disease free state. Disease free state is defined as no tumour mass was observed during the clinical evaluation, CA 125 values were within normal level and no evidence of metastasis was observed in radio-imaging methods (CT scan, Ultrasonogram). Disease free state was evaluated after 12 months of therapy. Toxicity profile was also observed.

Results :

When the chemotherapy was started, the level of CA-125 started declining in 13 patients and came down to 50% of the previous value at the end of second cycle and the CA-125 level came down to less than 35 U/ml after the end of three cycles of chemotherapy. The rate of decline of the level of CA-125 is shown in Figure-1. And this level came down to less than 10 U/ml in all 13 patients in the subsequent follow up. The decline rate of CA-125 after chemotherapy was 77%. Two patients did not respond to chemotherapy and considered as resistant and ultimately they died. Another two patients had an initial decline of CA-125 level but both of them showed a high level during subsequent follow up and ultimately they died. The details of the patients are shown in the following table (Table-I):

Table I

Sl.	Diagnosis	Stage	CA-125 level		Outcome
			Before Chemotherapy	After Chemotherapy	
1	Epithelial Ca	IV	500-1000 U/ml	-	Died during follow up
2	Germ Cell Ca	IV	100-500 U/ml	<35 U/ml	Disease free
3	Epithelial Ca	III	100-500 U/ml	Resistant	Died
4	Epithelial Ca	IIb	500-1000 U/ml	-	Died during follow up
5	Epithelial Ca	IIa	100-500 U/ml	<35 U/ml	Disease free
6	Epithelial Ca	III	500-1000 U/ml	<35 U/ml	Disease free
7	Epithelial Ca	IIa	500-1000 U/ml	<35 U/ml	Disease free
8	Epithelial Ca	IIa	<100 U/ml	<35 U/ml	Disease free
9	Epithelial Ca	IIa	100-500 U/ml	<35 U/ml	Disease free
10	Epithelial Ca	IIIc	500-1000 U/ml	<35 U/ml	Disease free
11	Epithelial Ca	IIIc	500-1000 U/ml	<35 U/ml	Disease free
12	Germ Cell Ca	III	100-500 U/ml	<35 U/ml	Disease free
13	Epithelial Ca	IIa	100-500 U/ml	<35 U/ml	Disease free
14	Epithelial Ca	III	500-1000 U/ml	Resistant	Died
15	Epithelial Ca	IIa	500-1000 U/ml	<35 U/ml	Disease free
16	Epithelial Ca	IIb	100-500 U/ml	<35 U/ml	Disease free
17	Epithelial Ca	IV	>1000 U/ml	<35 U/ml	Disease free

The remaining 13 patients responded dramatically and all of them became disease free and in each case, the CA-125 level came down to below normal. Those patients are clinically as well as biochemically disease free till now. The three year survival rate is 72%.

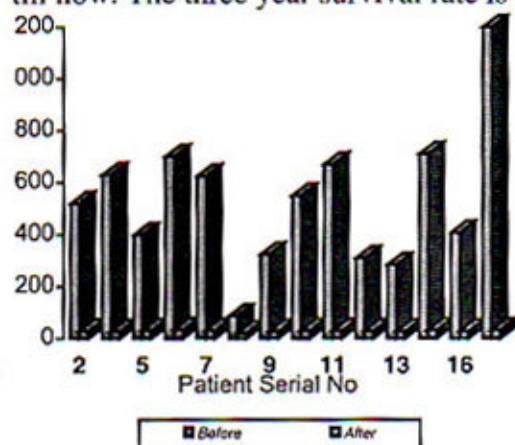


Figure-1: Response of CA-125 level following treatment

The patients who had an earlier decline of CA-125, responded better than others^{10,11}. And their outcome was good. But the patients who did not respond after starting of chemotherapy or showed an increase level of CA-125 after completion of chemotherapy during follow up period, eventually died¹². Another important finding is to be noted in this study that though CA-125 is a well recognized marker for epithelial type of ovarian carcinoma the level was also elevated in case of germ cell carcinoma before treatment. Both epithelial and germ cell cancer patients who responded to chemotherapy, the level of CA-125 declined subsequently.

Discussion :

CA-125 is a well-known tumour marker for ovarian malignancy, specially epithelial cell carcinoma. But there are some other non-malignant conditions where the level of marker can be increased such as endometriosis, pelvic inflammatory diseases, leiomyoma, adenomyosis, ectopic pregnancy, pancreatitis, cirrhosis of liver. The initial level of the marker along with the clinical signs plays an important role in diagnosing ovarian cancer. And the rate of increase of the level plays an important role in assessing the prognosis of the patient. It is a well-recognized marker for the epithelial type of ovarian malignancy. But in this study, it was also found that it has the same role in diagnosing and assessing the prognosis of ovarian cancer in germ cell type of ovarian malignancy. Seventeen patients with different types and stages of ovarian malignancy was enrolled in this study and all of them had a high level of CA-125. After the completion of chemotherapy, thirteen patients responded dramatically and their CA-125 level came down below normal. Two patients did not

respond at all to chemotherapy and was termed as resistant and ultimately, they died. Another two patients had an initial decline of the level but they died before completion of chemotherapy cycle. The outcome was good among the patients who responded to chemotherapy. So, the rate of decline of CA-125 level was proved as an important prognostic factor for the ovarian malignancy in this study.

CA-125 level plays an important role along with the clinical and imaging signs in diagnosing ovarian Cancer. But CA-125 test is not recommended for use alone as an early detection method of Ovarian Cancer, but rather with transvaginal sonography and rectovaginal pelvic examination for greater accuracy. Combining the detection methods lower the number of false positive² results. Usual imaging technique following surgery plays a less significant role in early detection of recurrence as well as in assessing the prognosis of the case, whereas the measurement of CA-125 level at regular interval, on the other hand, provides important clue regarding detection of early recurrence and assessment of prognosis of the case^{13,14}. This study showed that in these cases, the level of CA-125 came down within normal range and persisted within that range after chemotherapy with Taxotere-Carboplatin combination. The patients were well, disease free during the three years post-chemotherapy follow up. So, CA-125 has been proved to be a very significant tool in predicting the prognosis of ovarian cancer patients, who had chemotherapy or surgery.

Note :

- a. Docetaxel (Taxotere®) is a new taxoid, it enhances micro tubule assembly and inhibits depolymerization . Taxotere is a new chemical entity that inhibits cancer

cell division by essentially "freezing" the cell's internal skeleton, which is made of elements called microtubules. Taxotere acts on the internal skeleton by promoting the assembly and blocking the disassembly of microtubules, which prohibits cancer cell division and stops tumour growth. This action can lead to cancer cell death.

- b. A CA-125 test result of greater than 35 U/ml is generally accepted as being elevated. The test result of CA-125 may be of four categories. A true positive result is when the CA-125 test identifies a patient as having ovarian cancer and they do have ovarian cancer. A false positive result is when the CA-125 test identifies a patient as having ovarian cancer, and they do not have ovarian cancer. A true negative result is when the CA-125 test identifies a patient as not having ovarian cancer, and they do not have ovarian cancer. A false negative result is when the CA-125 test identifies a patient as not having ovarian cancer, but they do have ovarian cancer.

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