

**A Soujourn beyond Palliation of Stage 4 Ovarian Cancer: Case II****Dr. R.S. Ravi Chandra\***

Free-lance surgeon, India

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**Abstract:** This case report describes a patient diagnosed to have advanced Stage 4 Ovarian cancer malignancy on first visit during May 2015. Three major hospitals in Chennai had declared the case as inoperable and suggested only palliative chemotherapy and professed a bleak prospect, as the case belonged to stage 4b category and with Tumor marker CA 125 level being above 1000. However this case was operated and given an excellent recovery with complete remission within a short span of just 3 months, by a combination of surgery and Cryofreezing done on 21.5.2015, followed by a combination chemotherapy Immunotherapy and nutritional care. Patient attained complete remission by 1.8.2015 in a minor span of just 70 days with her CA 125 tumor marker level dropping down to below 35 within this period. A very minor relapse in one left iliac node with CA 125 again rising to 116 occurred in July 2016 after a lapse of 11 months, and was immediately dealt with by just cryofreezing of the node. No further chemotherapy was given. Tumor marker level returned to below normal level within a month and patient has absolute perfect remission till date, a period of well over 27 months. This case amply highlights the extreme usefulness of cryofreezing along with a multimodality approach which had affected a spectacular recovery of a declared inoperable case of very poor prognostic index.

**Keywords:** Multimodality approach, surgery and Cryofreezing, post-surgery relapse, repeat cryo freezing.

**INTRODUCTION**

Ovarian carcinoma is one of the silent killers of female patients. This high mortality is mainly due to the stealth appearance and progression to advanced stages without any symptoms and manifestations and thus rightly called the cancer that Whispers. This results in 75% of patients being in advanced stages III and IV when diagnosed first and thus accounting for poor prognosis. Despite advances in surgical techniques and chemotherapy including intraperitoneal chemotherapy popularly called HIPEC therapy, only modest improvement of overall survival of such patients is seen. The American cancer institute's statistical 5 year survival rate in stage IV invasive epithelial ovarian cancer is dismal 19% and another study fixes the figure at less than 10%. The modes of treatment adopted in such cases were cytoreductive surgery followed by combination chemotherapy or chemotherapy first followed by cytoreductive surgeries. These cytoreductive surgeries only meant physical removal as much possible of the tumor mass without endangering the patient's life by ruthless removal leading to torrential bleed and/or catastrophic dissemination.

These iatrogenic possibilities, limit the number of cytoreductive surgeries being taken up immediately, by declaring safely that the tumor is inoperable. To circumvent this negative tendency and to dramatically improve on the quantum of cytoreduction even in declared inoperable cases, it is imperative that we adopt cryofreezing. I sincerely wish that this approach is adopted by enterprising surgeons hence forth for the magnificent results seen.

**CASE REPORT**

Mrs.Saraswathy aged about 56 years was screened ultrasonographically for complaints of mild abdominal pain and slight distension of abdomen in the month of June 2015. Clinical exam revealed free fluid in the abdomen. Sono picture showed a bizarre transversely aligned mixed echogenic linear structure in the upper abdomen. There was also evidence of moderate ascites. Diagnostic ascitic tapping revealed blood stained fluid. Biochemical and cytology study revealed malignant effusion with cytology report pointing to adenocarcinoma.

**Microbiological  
Laboratory**

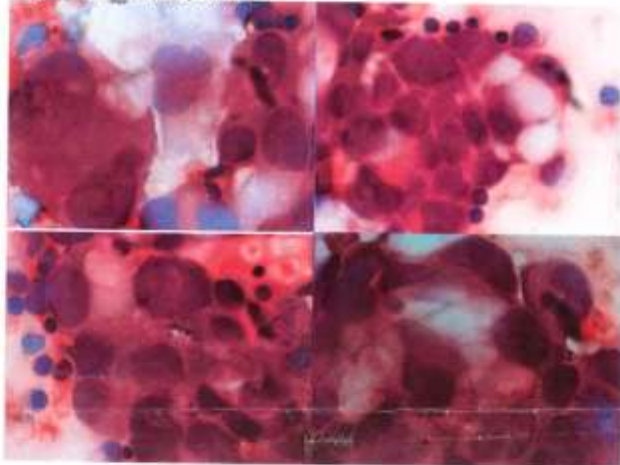
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**NICROBES**  
SINCE 1977

Bill ID : 02039019 Age: 56 y Receipt Date: 15.05.2015  
Patient Name : Mrs Saraswathi Report Date: 15.05.2015  
Ref. by Dr. : Dr P Nageshwara Rao

**Ascitic fluid Cytology Report**

Smears show numerous clusters of, as well as discrete malignant cells with cytoplasmic vacuoles, high nucleo-cytoplasmic ratio and prominent nucleoli. There are *no epithelioid cells*; no parasites.



**Opinion** Ascitic fluid cytology shows features that suggest a malignant effusion, compatible with adenocarcinoma. Biopsy confirmation is desirable.

**Dr. Krishna Venkateswaran, MD., DNB.,**  
Consultant Pathologist  
Microbiological Laboratory, Coimbatore

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Fig-1



**Fig-2**

Later whole body PET scan revealed the baffling stage of advanced state of disease, i.e. stage IV ovarian carcinoma, with metabolically active right infraclavicular nodes, internal mammary nodes, subcarinal and anterior cardiophrenic nodes in

thorax with malignant pleural effusion, which also revealed mild FDG uptake. In the abdomen, in addition to omental caking, there were multiple peritoneal nodules, enlarged aortocaval nodes and malignant ascites.

DEPARTMENT OF RADIOLOGY	
Patient's Details	Ms. SARASWATHY P [F] 56 Years
UHID	ASHI.000011522 Ward/Bed No. : OP /
I.P.No./MR No.	CNSOPP19309 Received on : 18-May-2015 11:49
DRN	315023904 Reported On :
Referring Doctor	SELF REFERRAL
<p align="center"><b>PET-CT WHOLE BODY</b></p> <p><b>PET-CT REPORT</b></p> <p><b>CLINICAL HISTORY</b></p> <p>Malignant ascites, for evaluation.</p> <p><b>CT FINDINGS</b></p> <p>Multislice (64 slice) serial axial sections of head to mid thigh were studied after administration of IV and oral contrast.</p> <p><b>BRAIN</b></p> <p>Cerebral parenchyma shows normal attenuation, enhancement and gray white matter differentiation. Brain stem and cerebellum are normal. Ventricles and cisterns are normal. Calvarium shows no destructive lesions.</p> <p><b>HEAD AND NECK</b></p> <p>Prominent bilateral level II cervical nodes are seen. No other significant cervical adenopathy seen. Base of skull, orbits, paranasal sinuses, nasal, oro- and hypopharynx and larynx are normal. Bilateral carotid arteries and jugular veins are normal. The parotid and submandibular glands are normal. Thyroid gland is normal.</p> <p><b>CHEST</b></p> <p>Moderate left pleural effusion seen with passive collapse of basal segments and lingular lobe. No evidence of pleural thickening or nodules seen.</p> <p>Enlarged right infra-clavicular, bilateral internal mammary and anterior cardio-phrenic recess nodes are seen; largest right internal mammary node measures 1.5 x 1.0 cms and right anterior cardio-phrenic recess node measures 1.2 x 0.8 cms.</p> <p>Prominent bilateral axillary nodes and subcarinal nodes are seen with preserved fatty hilum in the axillary nodes.</p>	
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<p align="center"><b>PET-CT WHOLE BODY</b></p> <p><b>PET REPORT</b></p> <p>Fusion PET/CT imaging was performed from the vertex of skull to mid thigh 60 mins after IV administration of 4.8 mCi of F-18 fluorodeoxyglucose (FDG). CT was performed for the purpose of attenuation correction and anatomical correlation. Blood glucose level was 122 mg/dl prior to scan.</p> <p><b>Head and Neck</b></p> <p>Physiological FDG uptake is noted in the head and neck. No significant FDG uptake is seen in the prominent bilateral level II nodes. No significant FDG avid supraclavicular nodes are seen.</p> <p><b>Thorax</b></p> <p>Increased FDG uptake is seen in the prominent right infraclavicular (SUVmax 2.7), internal mammary (SUVmax right 5.9) and left 3.5), subcarinal (SUVmax 3.1) and anterior cardiophrenic (SUVmax right 3.0 and left 2.8) nodes.</p> <p>Mild FDG uptake is seen in the left pleural effusion (SUVmax 2.0). No significant FDG uptake is seen in the prominent bilateral axillary nodes. No significant FDG axillary nodes are seen.</p> <p>No abnormal FDG uptake is noted in the lungs.</p> <p><b>Abdomen and Pelvis</b></p> <p>Increased FDG uptake is seen in the multiple nodular peritoneal thickening (SUVmax hepatic 5.9, left adnexa 4.5 and rectovesical pouch 6.4).</p> <p>Increased FDG uptake is seen in the omental caking (SUVmax 9.2).</p> <p>Increased FDG uptake is seen in the enlarged aortocaval (SUVmax 8.7) node.</p> <p>Mild FDG uptake is seen in the ascites (SUVmax 2.9).</p>	
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Fig-3

This advanced state obviously was declared inoperable and patient was advised to have three chemo

cycles first, by many leading oncologists who were also unanimous in portraying a poor prognostic picture.

#### ONCOLOGIST OPINION



Fig-4

In addition to the PET scan picture CA 125 was also above 1000, whereas value as low as 65 is considered to have very poor prognosis.

In this scenario a bold decision was taken to go ahead with cytoreductive surgery first. Laparotomy was performed on 20.5.15. On opening the abdomen, the whole picture was demoralizing with numerous metastatic nodules sparing no visceral surface. Still with great dexterity, first total omentectomy was done. Later, total abdominal hysterectomy with bilateral salpingo oophorectomy was completed. Ironically, both the ovaries looked almost near normal by external

appearance. In spite of these procedures, still there were innumerable malignant nodes over the mesentery, ligamentum teres, over the serosal surface of small and large bowel, a bigger one in the pouch of Douglas, etc. This is the situation where physical removal of these metastatic nodule which will be catastrophic or suicidal. And for this reason, such cases are declared as inoperable. The technique that comes handy in such a scenario is the use of cryofreezing. With extreme patience and dexterity every nodule was individually deep cryofreezed. Care taken to avoid cryo injury to the underlying vital viscera and major vessels.





**Fig-5**



**Fig-6**

No attempt was made to remove the frozen masses. Abdomen was closed as such. Patient had a smooth postoperative period. She was administered Inj.interferon alpha 2B from first post-operative day onwards. On the fifth post-operative day, she was given combination chemotherapy carboplatin and paclitaxel. The safe strategy of low dose high frequency

chemotherapy was adopted which resulted in almost zero side effects due to the chemo drugs. No hematological aberration or hepatorenal function aberration was encountered. There was absolutely no hair loss also. Patient remained healthy throughout the treatment period.



**Fig-6**



**Fig-7**

Tumor marker CA 125 level nose-dived steeply to reach below normal level within just 70 days, an unbelievable marvel.

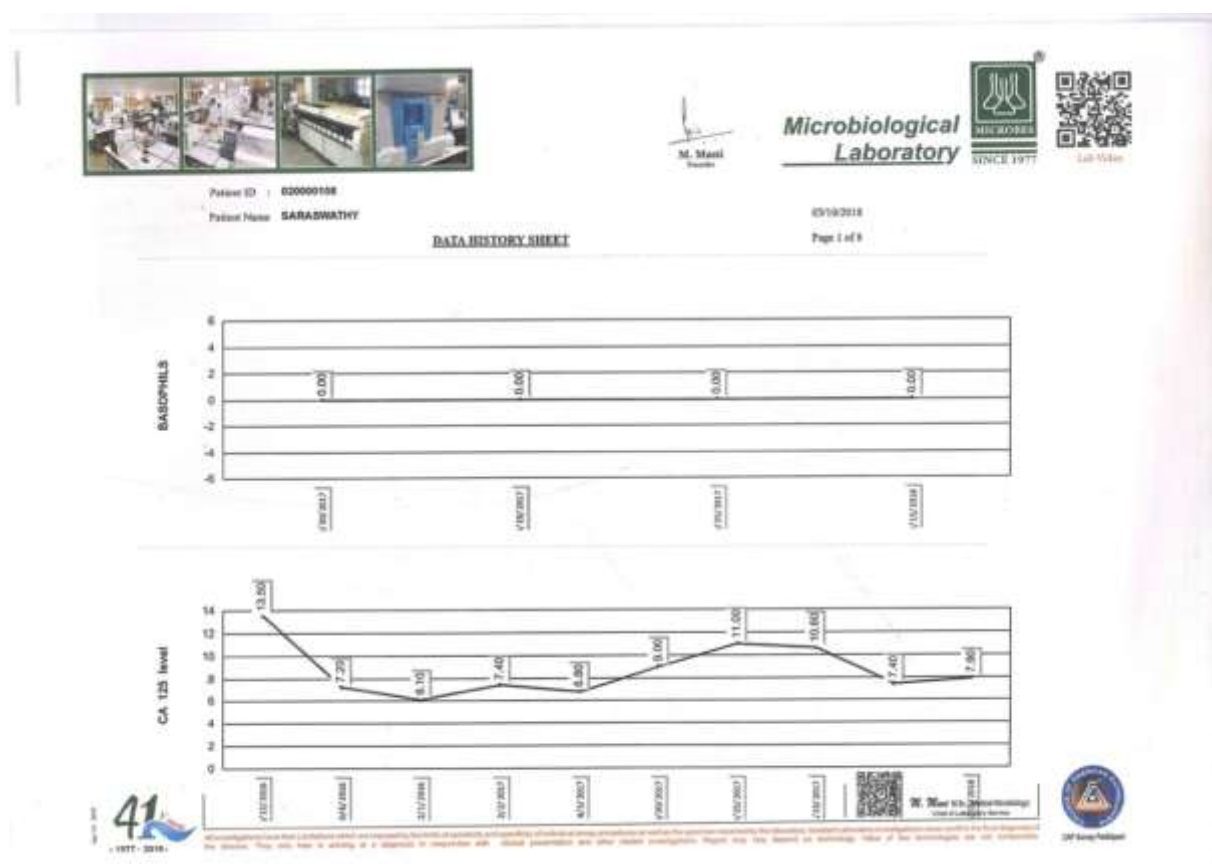
This perfect remission lasted for almost a year. Then a significant biochemical recurrence with CA 125 level reaching 116 on 1.07.2016 was seen. Repeat PET

scan revealed a single left iliac node which was metabolically active. Patient incidentally developed incisional hernia. Because of the hernia it was decided to go for surgery again. The only metastatic node was thoroughly deep cryo frozen. Mesh repair of the hernia done. No further chemotherapy was given. The tumor

marker level immediately dipped down to normal within a month, ie. on 12.08.16. From then on till date, there is a perfect state of complete remission, with tumor marker levels done periodically all showing values below 15 only. Patient is absolutely hale and healthy.

**Table-1: CA 125 levels and other hematological parameters during treatment**

DATE	CA 125 LEVEL	HB%	WBC COUNT	RBC COUNT	UREA/ CREATININE
5.6.2015	ABOVE 1000	10.3	6400	3.73	16/0.9
18.6.2015	716	10.4	4530	3.83	16/0.8
27.6.2015	230	9.8	7110	3.55	10/0.9
10.7.2015	115	10.1	7670	3.61	10/0.9
21.7.2015	46.5	10	7770	3.51	15/0.8
28.7.2015	33	10.3	7410	3.56	12/0.8
12.8.2015	19.7	10.5	8950	3.51	10/0.8
CHEMOTHERAPY STOPPED					
22.9.2015	13.7	11.4	7640	3.6	14/1.0
30.10.2015	7.5				
1.7.2016	116.5				
patient had a small iliac node, Metabolically active, and an incisional hernia. The node was just deep cryofreezed and Mesh repair of the hernia done. No chemo therapy given again. Just with cryo alone the CA 125 level started coming down.					
3.7.2016	82.5				
12.8.2016	13.5				
2017	9				
2018	7.9				



**Fig-8**



## **DISCUSSION**

Given the extensive intra-abdominal lesions with malignant pleural effusion, infra clavicular nodal and, supra diaphragmatic nodal metastasis, Onco Surgeons were unanimous in declaring this case as inoperable and advised only palliative chemo therapy first. Suggesting chemotherapy alone as the primary line of management in stage 4 has many pitfalls. No one can be sure that the tumor will be responsive to the chosen medicines. This will be known only after completion of at least 2 to 3 chemo cycles. This takes about 2 to 3 months' time. Suppose if the malignancy is chemo resistant and unresponsive to the chosen medicines, within this golden period the tumor can spread alarmingly beyond imagination. In such a scenario, we would be doing more harm than good to the patient, a situation I want to absolutely avoid. This will not be the case if we choose definitive surgery or Cytoreductive surgery first. If we can eliminate tumor load to the tune of 80-90%, then follow up chemotherapy, even if it fails, things will not go out of control, since in addition to chemotherapy, we will always be giving Immunotherapy simultaneously and also since the tumor load is minimal, we would have the breathing time to change the strategy and try a new chemo combination or choose Targeted therapies etc. In cyto reductive surgeries being done by Onco surgeons also there are a lot of shortcoming, for as in this case, if the disease is declared as stage 4, then most surgeons declare the case as inoperable. Even if some bold surgeons decide to go ahead with surgery, on seeing the enormous peritoneal seedlings as in this case they would have stopped proceeding further for such was the chaotic picture inside. This is because the operating surgeon only utilizes surgical ablative techniques, which will be possible only upto a certain stage of malignancy, beyond which it cannot be accomplished if the metastasis are sitting over intestinal serosa, or over the mesenteries, or over vital vessels. If still pursued in such a scenario then the surgery will be a real mess with either torrential bleed, or extensive iatrogenic dissemination, or chances of bowel perforation, or situations resulting in bowel resection and anastomosis. So fearing these possibilities the procedure will be usually abandoned. Here comes the invaluable use of cryotherapy. If by bold surgical techniques a cyto reduction of 50-60% is possible, the simultaneous use of cryofreezing can aid further cyto reduction to the extent of 90-95%. Minimal Residual Disease, defined as tumor deposit less than 1cm after cyto reductive surgery is a vital prognostic factor that depends on the caliber of the surgeon and the extent of cyto reduction accomplished. But the surgical fraternity, a vast majority, is clueless as to the means of achieving it. Certain set of surgeons adopt major radical procedures to achieve it, with all the associated morbidities. Certain others adopt fascinating procedures like Particle implantation intra lesionally. (Through minimally invasive approach, Radioactive material will be implanted into the tumor), sounds good but is it that

freely available and economic for every surgeon to go for it. In scenario like this patient, is it possible to implant dozens of radioactive particles intra abdominally. Recently a galaxy of newer medicines like Bevacizumab, Olaparib, Irenotecan, etc,etc have been used. Also new techniques like Intra peritoneal hyperthermic chemotherapy (HIPEC), intra-lesional chemotherapy have sprung up which have helped in better amelioration and survival but not without hitches. Bevacizumab, parp inhibitor Olaparib etc are extremely cost prohibitive and equally toxic. HIPEC procedure is very cumbersome and a recent study has shown that the possibilities of successfully accomplishing the HIPEC protocol would be very low below 42% as a result of severe systemic complications related to treatment.

But none of these procedures could match the results of this case obtained by adopting very simple non-lethal and cost effective multi-modality approach [1]. One more interesting case report by Zhen Huang, Devendra chavan, Dept of O&G, Qilu hospital of Shandong University, Jinan, briefs about a stage 4 Ovarian cancer patient being given a staggering 9 year survival duration looks heartening, her actual life should have been miserable. She had been literarily bombarded with all possible chemo medicines numbering around 20, and 57 cycles of chemo administered over 13 times spanning 9 years. A great clinical achievement, but not soul satisfying. Exorbitantly costly treatment, extreme chemical bombardment of the patient, not possible to emulate in all patients. The patient should have been a lion hearted soul. When compared to all these highly morbid approaches, and extremely costly procedures, my way of achieving maximum cyto reduction with surgery coupled with cryotherapy is matchless. This technique has helped me convert many declared inoperable cases and achieve maximum cyto reduction even to the tune of 95%. This magnitude of non-lethal cyto reduction helps the patient to a smooth post-operative recover, which in turn helps the patient to withstand chemotherapy and other treatment modalities easily. Thus economy wise and morbidity wise this cytoreductive approach is miles ahead of other procedures, but unfortunately not appreciated or adopted commonly. I pity the patients who are not given the benefit of this excellent tool, the cryoablation. This is not to take the credit off the present day inventions, which can very well be adopted in specific cases with much benefit. So a radical change in approach to management of advanced malignancies is very much essential, in the interest of the suffering millions.

## **CONCLUSION**

The world is still wading in the dark in management of stage 4 cancers. No single foolproof strategy has still been arrived at. In such a dark atmosphere even a candle's light must be whole heartedly acknowledged. Such is the utility of cryotherapy. The unmatched efficacy of this tool in

executing maximum cyto reduction with least toxicity deserves due consideration. For effecting cytoreduction one need not opt for exorbitantly costly and extremely morbid tools and procedures when a simple wonder tool is there. The real benefits of cryo cyto reduction or cryo ablation must be diligently probed further in a better scientific way for I have realized its true potential. It is a real game changer, most novel, most simple, most economic and least lethal amongst all the tools available for cancer management. It may also be playing a vital role in immune stimulation by providing to one's immune system frozen, avirulent, antigenically intact cancer cells. A dedicated research in this direction will one day prove my hypothetical assumptions, that cryotreatment is an immune stimulant. This would to a great extent pave way for the benefit of unfortunate advanced cancer patients. With cryotherapy, there is no question of inoperability. So other than medically unfit patients, for all other advanced cancer patients, cyto reductive surgery must be done first of course using to the maximum extent, non-lethal tools. In cryo freezing, it is just sufficient to freeze the pathology to the maximum safe limit as possible and leave it as such. The frozen tumor on its own melts away into oblivion, depending on the extent and effectiveness of our freezing. In this patient also when there was a necessity to reopen the abdomen for the sake of repairing incisional hernia, it was heartening to see absolutely

normal viscera without even a trace of those horrific frozen metastatic nodules, scarring or adhesions. The stunning clinical recovery in this patient by adopting the multi-modality approach strategy is there for all to see. Normal post-operative PET scan report and tumor marker level remaining continuously below 15ng/ml for well over 27 months post relapse, not requiring costly medicines, not requiring radiotherapy, not requiring HIPEC procedure, not requiring Targeted therapy and any other high end devices or medicines etc. This is a testimony to the supreme efficacy of multimodality approach, with cryotherapy as the main sheet anchor. Let this report enlighten the medical fraternity to adopt cryotherapy and achieve great feats as this case" A Sojourn beyond Palliation in Stage IV Prostatic Malignancy D [2]".

#### **REFERENCES**

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