



Original Article

AYURVEDIC THERAPEUTIC STRATEGY TO MAINTAIN LEVELS OF CA 19-9 MARKERS AFTER 5 YEARS OF POST-CHOLECYSTECTOMY FOR CARCINOMA GALL BLADDER: A CASE REPORT

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Abstract

Presenting a case has always been a fundamental way of sharing knowledge and conveying medical experience so that it can help the mankind and shape the way we see the problem of Cancer or malignancy from Ayurvedic point of view. It has been seen that many bioactive molecules have potential to interrupt carcinogenesis, specifically when they are of dietary and therapeutic origin in Indian system of Medicine. They come under category of nutraceuticals and play a vital role in overall well-being of the humans. The present case report is about such a case in which the patient was diagnosed with carcinoma gall bladder, for which cholecystectomy done and after 5 years of surgery, certain carcinogenic indicators (CA 19-9 markers) in body started increasing (84.15 U/ml) for which nutraceuticals based Ayurvedic management was adopted at OPD level at Ch. BrahmPrakashAyurvedCharakSansthan, New Delhi based hospital. The results of the therapy were promising as along with symptomatic relief, the CA markers level came down to 54.59 U/ml within 3 months. Prognosis of the case was acceptable as the patient was otherwise not showing any sign of active malignancy. It is a clinical experience based case report following the holistic approach of Ayurveda for chemoprevention.

Keywords: CA Gall bladder, Cholecystectomy, CA 19-9 markers, Cow urine, malignancy, Ayurvedic management

INTRODUCTION

The present case report is regarding a male cancer patient, who was diagnosed with carcinoma gall bladder in 2013 and was operated for carcinoma Gall bladder in 2013 with cholecystectomy. On taking the complete medical and personal history of the patient it was known that he was having habit of smoking till age of 35 then he stopped smoking. His bowel and bladder habits were normal. His environmental and occupational history was not remarkable. He was an employee in a private firm/office and had sitting desk job. His Blood pressure, pulse rate,

respiration rate was normal when his treatment was started. Patient had 21 BMI (Body Mass Index).

The patient was treated on the OPD basis and weekly follow up was done during the 3 months regimen. He was absolutely fine till June, 2018.

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Then he came to know that his Cancer Antigen 19-9 marker has started increasing remarkably which put the fellow in a fear of recurrence of his cancer.

This patient aged 46 years had approached the OPD of Ch. Brahm Prakash Ayurved Charak Sansthan Hospital, New Delhi in July, 2018. The patient came with the chief complaints of acidity, nausea and vomiting with generalized weakness. The patient came with his investigation reports of CA markers level, CT scan showing no signs of malignancy or metastasis and along with the case record of having been operated for carcinoma gall bladder in 2013. The patient wanted to take Ayurvedic treatment as his CA markers were increasing since June, 2018 while none of his CT scan reports showed any signs of remaining malignancy / metastasis in his body. Moreover he was told by his oncologist that until the malignant cells are seen in any of the part/organ of body the chemotherapy or radiotherapy for the same can not be started. Patient approached the hospital with complaints of dyspepsia since last 3-4 months and vomiting, nausea and acidity since last 7 years. The patient was prescribed all medicines from the dispensary of CBPACS and the treatment was continued for 3 months with weekly follow ups on outpatient department (OPD) basis. The results were miraculous as not only his CA markers level came down to 54.59 U/ml in September, 2018; but the patient was also having a feeling of well-being. CA (Carbohydrate Antigen) 19-9 markers are diagnosed by radioimmunoassay (RIA) test. Tumor markers are substances which are released by the cancer cells that can be sometimes present in the blood. The increased levels of CA markers give an indication about the developing cancer pathology and the stage of the present malignancy in body. The patient has responded very well to the Ayurvedic medical intervention in such a manner that has never seen before in regard of malignant cases.

Patient himself provided his case record with consent to present it as a case report. This case report provides a complete holistic approach in regard to physio-patho-pharma-therapeutic strategy about the case.

CASE REPORT

It is a newly written up experience of an interesting case. A male patient aged 46 years came to the OPD of CBPACS hospital in July, 2018 with chief complaints of acidity, vomiting and nausea since last 7 years. On taking the past history we came to know that the fellow was diagnosed with carcinoma gall bladder in July, 2013 on basis of CECT whole abdomen. He approached to Army hospital for the second opinion on the issue and was confirmed about his malignancy of gall bladder. The specimen for Histo-pathological examination (HPE) i.e. Biopsy confirmed the diagnosis of Carcinoma Gall bladder and Cholecystectomy was done for the same in August, 2013. The post-op, ultrasonography report showed status with clear gall bladder fossa and grade-I fatty liver. In September, 2017 another CT scan was done which was reported as "Post-cholecystectomy status with no evidence of any residual/recurrent lesion. Small contracted right kidney with chronic pyelonephritic changes and cystic lesions". In April 2018 one more CT scan was done to check the latest condition of the patient. The report of which revealed that liver was having decreased parenchymal attenuation but showed no signs of remaining malignancy or metastasis afterwards. The patient remained otherwise healthy till May, 2018. In June, 2018, patient approached to a nearby private hospital and got his CA markers level checked. The report showed very high level of CA 19-9 markers i.e. 84.15 U/ml. As the patient was not having any other sign of malignancy or metastasis on basis of the CT scan reports. So, no chemotherapy or radiotherapy was started for him for therapeutic purpose. Henceforth the patient approached for

an alternative therapy for his condition so that his chances of recurrence of cancer might be arrested considering the levels of CA 19-9 markers. As the high level of CA 19-9 markers put him in a fear of having malignancy again.

Investigations done in the course of disease	
6 th July, 2013 CECT Whole Abdomen	A poorly circumscribed intraluminal soft tissue attenuation mass is seen in GB, showing contrast enhancement. The plans of the mass with adjacent liver are ill-defined. Focal area of increased enhancement is noted in liver parenchyma adjacent to gall bladder fossa. There is no discrete focal hepatic parenchymal lesion. The G.B. mass also abuts the pyloroduodenal junction and the upper ascending colon. Generalized reduced liver parenchymal attenuation is noted, suggesting diffuse fatty infiltration. The intrahepatic biliary radicles are not dilated. Mild splenomegaly is seen with splenic length of about 13.5 cm. The right kidney is markedly shrunken with irregular cortical outline, suggestive of chronic pyelonephritic changes. Few small cystic lesions are noted in right kidney. A small calculus is seen in a lower pole calyx of left kidney measuring 2 mm. No evidence of hydronephrosis / uretric dilatation is seen. Portal vein, CBD, Pancreas, urinary bladder etc. normal.
30 th July, 2013 Biopsy Report (Gall Bladder for HPE) from Army Hospital	Well differentiated adeno carcinoma- Gall Bladder (1-11) <ul style="list-style-type: none"> • Background show tubulovillous adenoma • Mucin noted • No desmoplasia • No Lymphovascular emboli seen. • Tumour extends till muscular layer • No perineural invasion seen.
August, 2013	Cholecystectomy done
21 st August, 2013 Biopsy Report for HPE (Specimen: Nodal	1. Nodal clearance below head of pancreas: Free. No tumour deposit seen(1) 2. Lymphatic tissue from retroportal region: Eleven reactive lymph nodes seen. No

clearance below head of pancreas, lymphatic tissue from retroportal region, lymphatic tissue from hepatoduodenal ligament, lymphatic tissue from pericholedochal region, wedge resection of liver, cystic duct margin, port site tissue)	tumour deposit seen (2-3) 3. Lymphatic tissue from hepatoduodenal ligament: Two reactive lymph nodes seen. No tumour deposit seen (4-6). 4. Lymphatic tissue from pericholedochal region: Section show fibrocollagen, nerve bundles fat and blood vessels. No lymph nodes seen (9-8). 5. Wedge resection of liver: Section show maintained hepatic architecture with mild ballooning degeneration. Minimal portal inflammation noted. Granuloma with multinucleated foreign body giant cells also seen (9-12). No malignancy seen. 6. Cystic duct margin: Free. No tumour deposit seen (15). 7. Port site tissue :Free. No tumour deposit seen (16-17).
10 th June, 2017 USG Abdomen	Liver : 13.3 cm, shows diffuse grade I fatty infiltration. No SOL / IHBRD. CBD: Normal GB: Post cholecystectomy status. No recurrence or residual lesion seen in adjacent liver parenchyma. GB fossa clear. Spleen: Normal Pancreas : Obscured by bowel gas shadows. Right Kidney: 8.0X4.0 cm; increased cortical echogenicity with poorly maintained CMD. No PCS dilatation, 2 calculi of size 4.4 mm and 4.7 mm seen in midpole calyx. Left Kidney : 11X4.7 cm; Normal echotexture, PCS compact, CMD maintained, NO SOL/calculi U.B. :Well distended; Normal wall thickness. Prostate: 20.7 cc Normal 1. Post cholecystectomy status with clear GB fossa. 2. Grade I fatty Liver
13 th September, 2017 CECT Abdomen	Impression: Findings are suggestive of :- 1. Post chole cystectomy status with no evidence of any residual / recurrent lesion. 2. Small contracted right kidney with renal calculi and mild hydronephrosis.
30 th April, 2018 CECT Whole Abdomen	Spiral axial sections were acquired through abdomen after oral opacification of bowel before and after administration of I.V. contrast.

	<p>Status : Post Cholecystectomy</p> <p>Liver is normal in size and measuring 14.6 cm in craniocaudal dimension and shows decreased parenchymal attenuation suggesting fatty changes. No focal lesion seen. Intrahepatic biliary canaliculi and hepatic venous channels are normal.</p> <p>Gall bladder is not seen (post cholecystectomy). No recurrent / residual lesion notes at the post operative site. CBD is normal in caliber.</p> <p>Right kidney measures 6.1 cm and left kidney measures 11.4 cm in craniocaudal dimension. Right kidney appears smaller in size and reduced cortical thickness with compensatory enlargement in left kidney. However both kidneys are normal in outline, position and attenuation. Small focal hyperdensities are seen in right kidney measuring ~ 5-6 mm in diameter likely calculi. smld fullness also seen in right renal pelvis.</p> <p>Spondylo degenerative changes are seen in dorso-lumbar spine. Posterior marginal osteophyte formation seen at S1 level.</p>
6 th June, 2018 CA 19-9, Serum and Carcino Embryonic Antigen, Serum (Tumour Markers)	<p>CA 19-9 : 84.15 U / ml High (<1.20-30.90 U/ml)</p> <p>Carcino Embryonic Antigen : 2.68 High (Non smokers: < 2.50 and smokers : <5.00 ng/ml)</p>
14 th July, 2018 CT Whole Abdomen	<p>Liver: Normal in size (14 cm.). Parenchymal attenuation is normal and no area of differential enhancement is identified. Mild central IHBRD (Intra hepatic Biliary radicle dilatation) noted. Portal vein radicles are normal. Hepatic veins are normal. Main portal vein and branches are normal.</p> <p>GB : Not visualized (Post operated status)</p> <p>Pancreas, Spleen : Normal in size, attenuation and enhancement.</p> <p>Right Kidney : Shrunken is size and measures 5.0 3.6 cm. Pelvicalyceal system is dilated. Cortex is thinned out. Multiple small cortical cysts noted.</p>

	<p>Multiple small concretions (measuring 2-3 mm) seen in mid and lower parts.</p> <p>Left kidney : Normal in size (9.8 5.2 cm) and show normal enhancement. No focal lesion identified.</p> <p>Impression : 1. Shrunken right kidney with concretions.</p> <p>2. Small right paraumbilical hernia.</p>
14 th July, 2018 CA 19-9, Serum and Carcino Embryonic Antigen, Serum (Tumour Markers) Renal Function Test	<p>CA 19-9 : 64.70 U / ml High (0 - 37.00 U/ml)</p> <p>Carcino Embryonic Antigen : 2.47 High (Non smokers: < 2.50 and smokers : <5.00 ng/ml)</p> <p>Renal Function Test :-</p> <p>BUN (Blood Urea Nitrogen) : 9.5 mg / dl i.e. WNL</p> <p>S. Creatinine : 1 mg / dl i.e. WNL</p> <p>S. Uric acid : 6.73 mg/dl i.e. WNL</p> <p>S. Sodium : 144 mmol/L i.e. WNL</p> <p>S. Potassium : 4.48 mmol/L i.e. WNL</p> <p>S. Chloride : 105.5 mmol/L i.e. WNL</p>
24 th September, 2018 Liver Function Test	<p>S. Bilirubin total : 0.63 mg/dl (WNL as per reference range)</p> <p>AST/SGOT : 38 IU/L (WNL as per reference range)</p> <p>ALT(SGPT) : 66 IU/L (WNL as per reference range)</p> <p>S. Protein Total : 8.0 g/dl (WNL as per reference range)</p> <p>Albumin : 4.58 g/dl (WNL as per reference range)</p> <p>Globulin : 3.32 g/dl (WNL as per reference range)</p> <p>Albumin/Globulin ratio : 1.41 (WNL as per reference range)</p> <p>GGT : 14 U/L (lower borderline)</p>
24 th September, 2018 CA 19-9 Serum markers	<p>CA 19-9 : 54.59 U/ml (0.00 – 37.00 U/ml)</p>
7 th February, 2019 18F-FDG PET CT Scan of Whole body	<p>Impression : Whole body PET CT reveals :</p> <p>No scan evidence of any significant active disease in rest of the visualized segment of the body.</p>

The patient was given Ayurvedic prescription from the available medicines in the dispensary of C.B.P.A.C.S. hospital for 3 months with weekly follow ups. Keeping in mind the renal

condition of the patient no mineral or metallic based Ayurvedic composition was prescribed. The patient was advised the following medicines-

1. Cap Immuno care 2 TDS (Main ingredient Ashwagandha, Giloy, Safedmusli, Shatavari)
2. Sanshamnivati 2 TDS (Giloy + Ativisha)
3. Tab. M. Liv 2 TDS (Bhringraj, Bhumyamalki mainly with other herbs like Kasni, Raktpunatnava etc.)
4. M. Brahmi Rasayan 10 gm H.S. with milk (Brahmi mainly) to relieve stress)
5. Ark Ajwain 20 ml twice a day with warm water (Ajwain)
6. Cow urine 20 ml daily was given as adjuvant therapy (Cow urine)

HYPOTHETICAL ACTION OF FOLLOWING HERBS

The above mentioned regimen was prescribed to the patient, keeping in view his other medical conditions. The regimen included such medicines of Indian system of medicine which have been described and proved to be beneficial for enhancing the immunity and strength of the patient. The psychological status of the patient was also considered while prescribing the regimen as the malignancy itself is a psychosomatic problem and especially when there are chances of recurrence, the stress level of the affected person is doubled. In this case patient was under stress and anxiety about his health condition as the CA markers have started increasing, though any of the body scan was not showing any signs of malignancy in the body.

Henceforth such a regimen was prescribed to the patient that was having nutraceuticals functions along with therapeutic role in prevention of carcinoma by having immuno-modulator effects. To make the patient stress

free the medicine having anti-anxiety properties was prescribed.

The following herbs which were the major constituents of the prescribed formulations had contributed to the well-being of patient.

Ashwagandha (*Withaniasomnifera*):- It has been proved to be as an adaptogen, anti-inflammatory, anti-tumorigenic by virtue of its Immunogenic properties in Ayurveda¹.

Giloy(*Tinosporacordifolia*) :-

Isoquinoline alkaloids of stem root of 'Giloy' have exhibited anti-cancer, anti-inflammatory and immune-modulator qualities. It has also been proved beneficial in neurological and psychiatric conditions^{2,3}.

Shatavari(*Asparagus racemosus*) :-

Studies have shown that Asparagus could potentially induce cell apoptosis and G2/M cell cycle arrest in the more sensitive Hep3B and HepG2 cell lines in hepatocellular carcinoma. Studies have further revealed that deproteinized asparagus polysaccharide might exert its activity through an apoptosis-associated pathway. Thus Asparagus has exhibited significant anticancer activity against hepatocellular carcinoma cells, indicating that it is a potential therapeutic agent (or chemosensitizer) for liver cancer therapy⁴.

Bhringraj(*Eclipta alba*) :-

It has been revealed in a research that alcoholic extract of Ecliptaalba (AEEA) is effective in multiple cancer cell lines^{5,6}.

In another study Ecliptaalba has shown significant stimulatory effect on liver cell regeneration⁷. All extracts of Ecliptaalba were supposed to induce apoptosis in the cancer cells⁸ and crude methanol extract of Eclipta alba has been shown to inhibit growth of colon cancer cells⁹.

Bhumyamalki(*Phyllanthusniruri*) :-

Studies have revealed that preclinical pharmacological activity and therapeutic potential of phytochemicals isolated from *Phyllanthus niruri*¹⁰. The species has demonstrated an antimutagenic and

anticarcinogenic action, antitumor¹¹, antioxidant¹², hepatoprotective^{13,14}.

Brahmi (Bacopamonierra) :-

A study is reported on the effects of Brahmi (Bacopamonierra) on human memory. The results showed a significant effect of the Brahmi on a test for the retention of new information¹⁵. Bacopa may increase the effects of many key neurotransmitters such as Acetylcholine, noradrenaline, serotonin and dopamine which are the cause of calmness & mood regulators. Bacopa has shown significantly results in cases of anxiety and depression^{16,17}.

Ajwain (Trachyspermumammi) :-

The studies have shown that ajwain seeds are bitter and pungent in taste and acts as anthelmintic, carminative, laxative and stomachic. It also cures abdominal tumours, abdominal pains and piles¹⁸.

Cow urine :-

Many studies and researches have been conducted on cow urine in reference to its effect on cancer patients by using it orally as an adjuvant therapy.

Recent researches have shown that cow urine is antifungal, anthelmintic, antineoplastic in action. It is also useful in hypersensitivity reactions and increasing the life-span of a person. It is immuno-modulator also. Cow urine possesses antioxidant properties which are because of uric acid and allantoin present in it. Hence it is having anticancer effect. It is further mentioned that daily consumption of cow urine improves immunity due to allantoin¹⁹.

After starting the above treatment, in July, 2018 another CT scan was done to check the condition of the patient, no sign of malignancy or metastasis was seen in the body. It again reported small right para-umbilical hernia and shrunken right kidney with concretions. This condition was present earlier also when patient approached for Ayurvedic treatment.

After a course of two weeks therapy, in July, 2018 the level of CA 19-9 markers started falling (reported 64.70 U/ml) and it continued. In the end of September, 2018 once again CA 19-9 markers were tested which came out to be 54.59 U/ml i.e. the level continued falling.

The given regimen was found to be quite effective after follow up of one week and patient started giving good response to the regimen. After completing the course for three months, there was significant fall in the increased level of CA 19-9 markers and patient showed improvements in the symptoms of acidity, nausea and vomiting with which he approached for alternative system of medicine. Subsequently, the patient was also suffering from renal calculi and concretions with hydronephrosis in right kidney. Hence, when his CA 19-9 marker level started falling and reached 54.59 U/ml (Normal is upto 37 U/ml) and patient showed interest in consulting nephrologist for the condition of kidneys. He was suggested to continue the prescribed medicines till his CA 19-9 markers level reach within normal range.

AVAILABILITY OF DATA & MATERIAL

The source of available data and material is the medical reports (old and new all) and history given by the patient along with the prescription slips of the previous hospitals to which he consulted and got operated. Prescription slips of current prescription and its follow up along with investigation reports.

DISCUSSION

Patient was prescribed the therapeutic regimen as mentioned in Case Report. After the examination of patient, it was hypothesized that the Carbohydrate antigen (CA) 19-9, which are present in the blood and are wandering through-out the body via circulation of blood and are supposed to be present in blood only in the presence of malignant cells in the body. Basically, antigens are substances that cause the immune system to respond. This clearly says that if any antigen is present in the

body, the immune system will respond to it. If immune system is weaker, disease will occur and if immunity is strong, the disease might not happen. With this hypothetical reasons, the patient was treated with immuno modulators, anti-oxidants, anti-anxiety, hepatoprotective and rejuvenative formulations so that those wandering antigens (Carbohydrate Antigen i.e. CA 19-9) can not affect any weak part / site of body. It has been beautifully explained by Ayurvedic scholar Acharya Sushruta in the following verse²⁰ :-

“Kupitanam hi doshanamshariparidhaavatanm, yatra sangakha- vai-gunyatyadhihtatraupjayte”

It means the vitiated doshas are freely wandering in the body. Wherever they find the site susceptible to disease, doshas locate at that site, generate pathological changes and initiate the disease process. Basically, this verse comprises of 2 words: Kha- akasha, Srotas (micro-channels) and Vaigunya means Vigunata/Vikruti. Altogether Srotovaigunya means that condition of Srotas which is susceptible for pathological changes or favourable movement to produce a disease.

Further, the commentator Dalhanahas commented on this verse that prakupita (vitiated) doshas will be moving in the body produces disease after lodging in srotovaigunya and dosha-dushya-sammurchana. ***“KhavaigunyatitiSrotoVaigunyatitiartaha”***.

Srotovaigunya stands for some inherent weakness or lack of natural immunity to some particular disease or susceptibility to a particular disease. This can also be simplified that loss of resistance to disease producing factor can cause disease any time. In fact Srotovaigunya need not necessarily produce any disease, here we can say that increased levels of CA 19-9 markers can lead to srotovaigunya, but in later reports malignant cells are not yet found, this might be due to lack of dosha-dushyasammurchana. Therefore no such clinical manifestation of the recurrence of malignancy was noticed in the patient

inspite of increasing CA 19-9 markers. This was the hypothetical reason to give immune-modulators and rejuvenators to patient along with herbs for symptomatic relief. The patient showed good response to the therapeutic management and the reports justified continuous fall in the increased levels of CA 19-9 markers since the Ayurvedic treatment was started for him.

The effect of this regimen for management of post malignancy and post operated was good. Patient not only showed fall in the CA 19-9 markers level but also showed improvement in the associated symptoms. As per the patient, he was perfectly fine since last five years 2013 (from cholecystectomy) to 2018. He didn't show any sign of disease progression for last 5 years. But in 2018 when his CA 19-9 markers level came high, he developed a fear of recurrence of his malignancy. CT scan report showed that no malignancy / malignant cell / metastatic cell is found in the body but renal concretions of right kidney persist as earlier. Due to the psychological impact and fear of the patient for recurrence of cancer, the patient approached for alternative system of medicine i.e. Ayurveda at Ch. Brahm Prakash Ayurved Charak Sansthan Hospital, Khera Dabar, Najafgarh, New Delhi-110073.

CONCLUSION

The patients with increased Ca 19-9 markers level have the chances of recurrence of malignancy or its metastasis. But the CT scan report didn't indicate any signs of recurrence of malignancy in the patient. The only frightening sign was three times increased levels of Cancer Antigen 19-9 markers in the blood. Patient responded well to the Immunomodulators and antioxidants based therapeutic regimen. The fear of redeveloping the cancer, made the patient psychologically disturbed too. Hence the overall holistic approach of Ayurveda and proper therapeutic regimen including of Immuno-modulating effect, Anti-oxidant action, Antipyretics, Hepatoprotective drugs,

anti-anxiety medicine and anti-spasmodic medicines provided him good and quick relief and has been proved effecting in regulating the CA 19-9 marker levels with symptomatic relief. Appropriate treatment in this state i.e. before *sthanasamshrayaavastha* (manifestation of disease) of patient's condition has arrested the occurrence of next *avastha* i.e. chances of recurrence of malignancy.

ACKNOWLEDGEMENTS :

The author shows gratitude to the Institute and hospital authorities of Ch. Brahm Prakash Ayurved Charak Sansthan, Khera Dabar, New Delhi, as the medicines were provided to patient from the hospital dispensary itself and thank the patient for giving consent and showing his faith in Ayurveda, patience and obedience during the course of the treatment.

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