



Case Report

Long-Term Progression-Free Survival of Stage IV Triple Negative Breast Cancer Patient having Genetic Mutation with Variant of Uncertain Significance and Lung Metastasis: A Case Report Emphasizing Role of Ayurvedic Treatment

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Citation: Sardeshmukh SP, Deshmukh VV, Kulkarni AV, Godse VR, Datar SM, et al. (2022) Long-Term Progression-Free Survival of Stage IV Triple Negative Breast Cancer Patient having Genetic Mutation with Variant of Uncertain Significance and Lung Metastasis: A Case Report Emphasizing Role of Ayurvedic Treatment. Curr Res Cmpl Alt Med 6: 161. DOI: 10.29011/2577-2201.100061

Received Date: 9 September 2022; **Accepted Date:** 14 September 2022; **Published Date:** 19 September 2022

Abstract

Long-term progression free survival of 10 years 7 months was achieved in aggressive Triple Negative Breast Cancer (TNBC) with lung metastasis (Stage IV) in Indian female patient having Variant of Unknown Significance (VUS) mutation treated with 2 surgeries followed by adjunct chemotherapy by giving Ayurvedic treatment after completion of conventional treatment. It consisted of Oral Ayurvedic Medicines (OAM) and a periodic detoxifying procedure of Panchakarma for 10 times. The selected OAM report immunomodulatory, hepato-protective, anti-inflammatory and to certain extent anti-cancer activity.

The patient was diagnosed as right breast TNBC infiltrating duct carcinoma of grade III in May 2008, operated with Right Modified Radical Mastectomy with axillary clearance followed by 6 cycles of chemotherapy during June to October 2008. Patient was disease-free till March 2011; however, then she had gradually aggravated frequent episodes of cough with expectoration and hemoptysis. Computed Tomography (CT) Scan guided biopsy of left lung mass done in April 2011 revealed metastatic carcinoma consistent with a known primary in the breast. In May 2011, left lung upper lobectomy performed for lung metastasis, depicted

poorly differentiated metastatic carcinoma by Histopathology Report (HPR). She was again treated with 6 cycles of chemotherapy during June to September 2011. Patient is under Ayurvedic treatment at ICTRC since October 2011, after completing 2nd line conventional treatment. The investigative analysis done in 2022 indicates normal hematological, biochemical, radiological and clinical profiles suggesting disease control and improved quality of life based on QLQ questionnaire. Progression-Free Survival (PFS) of 10 years 7 months is reported in this patient.

Keywords: Ayurvedic treatment; Long-term progression-free survival; Lung metastasis; Panchakarma treatment; Stage IV breast cancer; Triple negative breast cancer; VUS genetic mutation

Introduction

Breast cancer has ranked topmost cancer with age adjusted rate as high as 25.8 and mortality 12.7 per 100,000 Indian females. Young age is a major risk factor for breast cancer in Indian women [1]. TNBC is a sub-type of breast cancer lacking expression of Estrogen Receptor (ER), Progesterone Receptor (PR), and Human Epidermal Growth Factor (HER2); and has an aggressive natural history and worse disease-specific outcomes compared with other breast cancer sub-types [2]. These patients are also known for an early recurrence between 1-3 years after diagnosis, and more aggressive metastases are likely to occur in viscera, particularly in the lungs and brain, and less likely to spread to the bones.

Present case includes a patient having Stage IV TNBC with Variant of Unknown Significance (VUS) genetic mutation, post Right Modified Radical Mastectomy (Rt-MRM) with axillary clearance, post Left Lung Upper Lobectomy and post chemotherapy for primary malignancy and lung metastasis. We hypothesize that the Ayurvedic treatment of a combination of oral herbo-mineral metallic medicines and periodic detoxifying procedures of Panchakarma given to this patient has provided Progression-Free Survival (PFS) of 10 years 7 months and good Quality of Life till date.

Case Report

Patient Information and Clinical Findings

A female patient of 41 years diagnosed as Infiltrating Duct Carcinoma (IDC), Grade III, Bloom – Richardson’s score 8, Stage II (Rt. Breast) on 15/05/2008 [Supplementary file 1], operated for Rt-MRM with axillary clearance on 21/05/2008 and immunohistochemistry confirmed as TNBC on 23/05/2008 [Supplementary file 2]. Patient underwent 6 cycles of chemotherapy (3 cycles of CEF – Cyclophosphamide, Epirubicin, 5-Fluorouracil and 3 cycles of Docetaxel) during June to October 2008. Patient was asymptomatic till March 2011. Thereafter, she had gradually aggravated frequent episodes of cough with expectoration and hemoptysis. Computed Tomography (CT) scan (Chest) dated 13/04/2011 revealed lobulated mass lesion involving anterior segment of left upper lobe of lung. CT guided biopsy of left lung mass on 20/04/2011 confirmed lung metastasis consistent with a known primary in the right breast. Left lung upper lobectomy was performed on 04/05/2011. Histopathology report (HPR) revealed metastatic poorly differentiated carcinoma with absence of metastatic deposits in mediastinal and inter-lobar nodes [Supplementary file 3]. Patient underwent 6 cycles of chemotherapy during June to September 2011 (Inj. Paclitaxel and Inj. Carboplatin). Genetic analysis of the patient detected VUS mutations on 31/07/2017 [Supplementary file 4].

Ayurvedic Treatment

The patient has been treated with Oral Ayurvedic Medicines along with yearly Panchakarma treatment (10 times) for detoxification from October 2011 till date at ICTRC, Wagholi, Pune as given in Table 1 and Fig. 1.

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Protocol set	Medicines with dose and vehicle	Duration
1	<ul style="list-style-type: none"> Atharva Suvarna Bhasmadi Vati (ASBV) (Patent published, Indian Patent application no. 201921018272 US Patent application no. 17/609,535) 395 mg with cow's ghee after breakfast and evening snacks Atharva Shatavari Kalpa [FDA, M.S., Product No. 417898] 5 g with cow's milk after breakfast and evening snacks Aarogya Vardhini Vati (AV) [3] 500 mg with lukewarm water after lunch and dinner Triphala Guggul (TG) [4] 500 mg with lukewarm water after lunch and dinner 	2 years 7 months
2	<ul style="list-style-type: none"> Atharva Suvarna Bhasmadi Vati (ASBV) as above Atharva Shatavari Kalpa As above Liv-Atharva Liquid (LA) [FDA, M.S., Product No. 418211] 10 ml with 50 ml of water after lunch and dinner Pippalyadyasav (PLA) [5] 10 ml with 50 ml of water after lunch and dinner 	1 year 8 months
3	<ul style="list-style-type: none"> Atharva Suvarna Bhasmadi Vati (ASBV) as above Atharva Aloe Plus Tab [FDA, M.S., Product No.418169] 500 mg with lukewarm water after lunch and dinner Atharva Ostopix Tab [FDA, M.S., Product No. 418160] [Patent application no. 202221023824] 500 mg with lukewarm water after lunch and dinner 	3 years 2 months
4	<ul style="list-style-type: none"> Atharva Suvarna Bhasmadi Vati (ASBV) As above Kamdudha Vati (Mouktikyukta) [6] 500 mg with milk after breakfast and evening snacks Atharva Ananta Vati [FDA, M.S., Product No. 418107] 1 g with lukewarm water after lunch and dinner Tab Prasham* 500 mg with lukewarm water after dinner 	1 year 8 months
5	<ul style="list-style-type: none"> Atharva Suvarna Bhasmadi Vati (ASBV) as above Kamdudha Vati (Mouktikyukta) as above Liv-Atharva Liquid as above Pippalyadyasav as above 	1 year 6 months

*Manufactured by Ayurved Rasashala, Pune, while rest of the medicines by Atharva Nature Healthcare Pvt. Ltd., Pune

Table 1: Protocols of adjunct Ayurvedic treatment with duration used in the present case study.

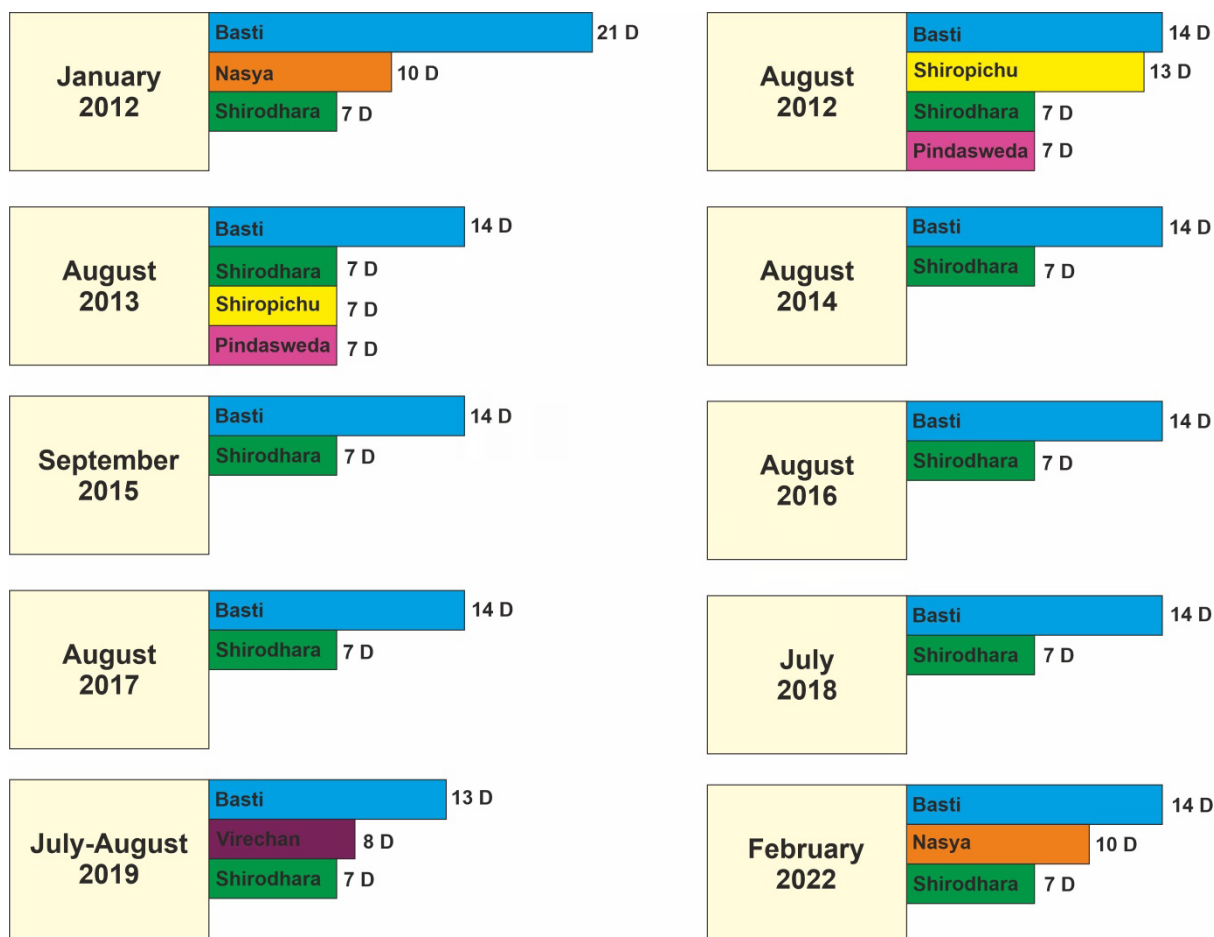


Figure 1: Timeline and duration in days (D) of Panchakarma procedures, viz., Basti (medicated enema), Virechana (inducing purgation), Nasya (nasal instillation) and allied procedures, viz., Shirodhara, Shiropichu (oil-based procedures of head massage) and Pindasweda (sudation performed using bolus of drugs) given to the patient under study.

Outcome and Follow-Up

Patient is under regular monthly follow-up at ICTRC for the last 10 years and 7 months. The side effects of chemotherapy, such as nausea, vomiting, diarrhoea were absent, while constipation and fatigue seen at the beginning of OAM treatment vanished within 3 months. For ease of assessment, her yearly follow-up in terms of clinical examination; haematological, biochemical and radiological investigations are given in Table 2, which clearly indicates disease control and gradual improvement in these parameters.

Time points→	A	B	C	D	E	F	G	H	I	J	K	L	M
Status and duration of OAM→	End of chemotherapy and beginning of OAM	3 months after end of chemotherapy and beginning of OAM	1 Y	2 Y	3 Y	4 Y	5 Y	6 Y	7 Y	8 Y	9 Y	9.5 Y	10.33 Y
Month / Year →	Oct 2011	Jan 2012	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Assessment parameters ↓													
A) Clinical parameters													
Weight	66	69.5	74	80	76	73.3	73.3	71.6	75.2	75.2	75.5	74.9	77.4
Karnofsky Score (KPS)	80	90	90	90	90	90	90	90	90	100	100	100	100
Functional Score from QLQ C30	84	98	98	98	96	96	100	93	100	100	100	100	100
Symptom Score from QLQ C30	8	3	3	3	0	0	0	0	0	0	0	0	0
Global Score from QLQ C30	67	100	100	100	92	100	100	83	100	100	100	100	100
Breast Score from QLQ BR 23	27	27	26	26	19	20	19	19	20	20	26	26	26
B) Radiological parameters													
X ray Chest	Prominent broncho-vascular margins	---	Post-operative status with port <i>in situ</i>	No abnormality detected (NAD)	---	Chemo port <i>in situ</i> . Clear lung fields	NAD	Mild prominence of broncho-vascular markings in bilateral lower zones	Unremarkable lung fields	---	---	NAD	NAD
USG abdomen and pelvis	Fatty Liver	Hepatomegaly with fatty changes	Fatty Liver	Fatty Liver	---	Moderate fatty liver	Fatty Liver	Mild hepatomegaly with grade II fatty liver	Hepatomegaly with fatty infiltration	Mild hepatomegaly with grade I fatty liver	---	---	Persistent mild hepatomegaly with grade I fatty liver. Rest NAD
C) Haematological and biochemical parameters													
Hb *(12-16 g/dl)	9.7	10.50	---	---	---	11.9	---	12.3	13	---	12.9	---	12.2
WBC *(4000-11000/cumm)	3031	4000	---	---	---	6160	---	6900	6200	---	7970	---	4560
Platelets *(150000-450000/cumm)	229000	275000	---	---	---	329000	---	306000	271000	---	284000	---	267000
S. Bilirubin *(0-1.2 mg/dl)	---	0.71	---	---	---	0.33	0.69	---	0.19	---	0.52	---	0.5
SGOT *(0-31 U/I)	44	26	---	---	---	21	21.41	36	18	---	20.9	---	18.2
SGPT *(0-32 U/I)	35	20	---	---	---	27	15.73	34	14	---	8.7	---	14.8
S. Alkaline phosphatase *(44-147 U/I)	---	49	---	---	---	63	63.77	---	73	---	82.7	---	62.9
S. Creatinine *(0.7-1.7 mg/dl)	0.8	0.98	---	---	---	1	0.98	0.85	0.82	---	0.76	---	0.77

Time points→	A	B	C	D	E	F	G	H	I	J	K	L	M
Status and duration of OAM→	End of chemotherapy and beginning of OAM	3 months after end of chemotherapy and beginning of OAM	1 Y	2 Y	3 Y	4 Y	5 Y	6 Y	7 Y	8 Y	9 Y	9.5 Y	10.33 Y
S. Urea *(13-43 mg/dl)	17	---	---	---	---	---	15.44	---	---	---	18.7	---	---
CA 15.3 *(0-32 U/ml)	29.5	---	---	---	---	15.4	13.87	23	---	---	---	---	26.60
CRP *(0-6 mg/l)	---	---	---	---	---	---	---	---	1.97	---	---	---	4.7
*Indicates normal range of haematological and biochemical parameters													

Table 2: Periodic clinical, radiological, haematological and biochemical evaluation of the patient

Reports of blood biochemistry investigations done in the last 3 years (2020-22) reported all the parameters within normal range (Table 2). Chest X-ray in January 2022 while USG (Abdomen and Pelvis) and Unilateral Mammography in February 2022 were also normal. Moreover, Magnetic Resonance Imaging (MRI) of brain and Electro Encephalogram (EEG) in December 2020 did not show any evidence of cancer metastasis. Patient is disease-free for the last 10 years 7 months and enjoys good quality of life. Patient's Karnofsky Score increased to 100 after continuous Ayurvedic treatment during the last four years. Quality of Life assessed periodically using QLQ C30 and QLQ BR23 revealed increase in Functional and Global score and decrease in Symptom score of QLQ, are also indicative of improvement in her well-being due to cancer control. In the 6th year of OAM, it was observed that weight, and functional and global scores of QLQ decreased (Table 2). Patient was hospitalized during this period (from 29/10/2017 to 13/11/2017), due to fever with chills, weakness, body-ache, myalgia and vomiting. Investigations depicted marginally raised SGOT and SGPT levels, mild prominence of broncho-vascular markings in bilateral lower zones in Chest X-ray and mild hepatomegaly with grade II fatty liver in USG abdomen and pelvis. A chemo port infection was suspected and the patient was relieved of symptoms after removal of the port.

During the 2nd wave of SARS-CoV-2 pandemic in India, this patient had low grade fever (99.5 0C) with chills and loss of smell on 10/03/2021 and her RT-PCR test performed on 13/03/2021 was positive [Supplementary file 5]. Patient was home quarantined for 14 days. Haemogram, Liver Function Test and CRP levels dated 11/03/2021 were within normal range and Chest X-ray done on 12/03/2021 was normal. In spite of her aggressive disease, TNBC with lung metastasis, she had minor symptoms of SARS-CoV-2 and recovered within few days without hospitalization. While her daughter, the co-resident, was also detected with SARS-CoV-2 infection during this period but suffered from high grade fever (3 days), cough, cold, loss of taste and smell, and her High Resolution-CT score 22/25 suggested lung congestion. Thus, the severity of SARS-CoV-2 symptoms in the case study patient was less and recovery was faster without any complications as compared to her daughter.

Discussion

India has been reported to have a rising incidence of breast cancer. Approximately, 10–15% of breast carcinomas are known to be of TNBC sub-type, characterized by onset at a younger age, high mean tumour size and higher-grade tumours. It is aggressive, associated with poor prognosis and high risk of relapse with short PFS and overall survival (OS). Metastatic TNBC patients have even shorter PFS and poor survival after recurrence. The median time from recurrence to death and survival time for metastatic disease is about 9 and 13 months, respectively; compared with 20 months for patients with other sub-types of breast cancers. Younger age at diagnosis (i. e. <50 years), early menarche and young age at the time of first child birth, are some of the risk factors of TNBC [7].

In the present case, the patient was diagnosed with grade III and Stage IIA (T2N0M0) TNBC at early age of 41 years and the high-risk factors like early menarche at the age of 11 years and the 1st delivery at younger age i.e., 23 years were also reported. After early peak of recurrence in the left lung within 3 years and completion of surgery and chemotherapy for lung metastasis, the sole treatment with Ayurvedic modality at ICTRC since 2011 led to PFS for 10 years 7 months in this patient. This is much higher than the reported PFS in the relapsed and/or metastatic TNBC.

TNBC patients with lung metastasis have been reported to have the maximum median post-metastatic OS of 16.6 (10.3-22.9) months. Also, the post recurrence (lung, brain, liver, bone metastasis) survival and the relapse free survival (RFS) of 3 and 5 years are only 20% and 8%, respectively [8]. In this scenario, PFS for 10 years 7 months after lung metastasis in the present case can only be attributed to correctly chosen Ayurvedic treatment comprising combination of OAM in 5 sets (Table 1) and frequent Panchakarma treatment (Figure 1). OAM was in the form of Dosha - Dhatu alleviating (Shamana chikitsa) and immunomodulatory (Rasayana chikitsa) treatment in the form of various combinations of herbs, minerals and metals. Shamana chikitsa is beneficial for maintaining equilibrium of Dosha and Dhatu by improving appetite and digestion, reducing generalized toxicity, imparting anti-inflammatory effects and improving quality of life. Rasayana chikitsa, additionally, exerts immunomodulatory effect and strengthens Dhatu. Panchakarma treatment detoxifies body by eliminating vitiated Dosha. Various reported uses of these specific medicines and their constituents are summarised in Table 3, while the important rationale in selecting these combinations is discussed below.

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Sr No	Medicines with constituents	Biological activities of and rationale behind selection of medicines
1	<p>Atharva Suvarna Bhasmadi Vati (ASBV) -</p> <p>Suvarna Bhasma (Incinerated Gold, a metallic preparation), Mouktik Bhasma (Incinerated Pearl, a Mineral), Guduchi Satva (Starch preparation of herb – <i>Tinospora cordifolia</i>)</p>	<ul style="list-style-type: none"> • Suvarna Bhasma – Immunomodulator (Rasayana), vitality enhancer (Ojovardhan), possesses detoxifying property (Vishapaha), improves appetite and digestion (Deepana and Pachana), thus promotes proper nourishment (Bruhana) [9], anti-oxidant activity, immune-stimulant activity [10] • Mouktik Bhasma - Pitta pacifying and cooling property [9], Anti-ulcer and anti-oxidant activity [11] • Guduchi Satva – Immunomodulator (Rasayana), improves appetite (Deepana), strengthens the body (Balya), eliminates excessive heat and burning sensation (Dahanashak) and is beneficial in anaemia (Pandu) [12], anti-proliferative activity, anti-cancer activity [13]
2	<p>Atharva Shatavari Kalpa</p> <p>Shatavari (<i>Asparagus racemosus</i>)</p>	<ul style="list-style-type: none"> • Immunomodulatory (Rasayana) • Anti-inflammatory effect (Shothanashak) • Increases strength by improving appetite and digestion. Improves functions of female genital organs especially of mammary glands and thus, effective in various breast disorders including breast cancer [12] • Anti-cancer activity [14]
3	<p>Aarogya Vardhini Vati (AV)</p> <p>Kajjali (Black sulphide of mercury) Loha Bhasma (Incinerated Iron) Abhrak Bhasma (Incinerated Mica) Tamra Bhasma (Incinerated Copper) Haritaki (<i>Terminalia chebula</i>) Bibhitaki (<i>Terminalia bellirica</i>) Amalaki (<i>Emblica officinalis</i>) Shilajit Shuddha (Black bitumen purified) Guggul Shuddha (<i>Commiphora wightii</i>) Chitrak (<i>Plumbago zeylanica</i>) Kutki (<i>Picrorrhiza kurroa</i>) Nimba (<i>Azadirachta indica</i>)</p>	<ul style="list-style-type: none"> • Hepato-protective activity [3,15]
4	<p>Triphala Guggul (TG)</p> <p>Haritaki (<i>Terminalia chebula</i>), Bibhitaki (<i>Terminalia bellirica</i>), Amalaki (<i>Phyllanthus emblica</i>), Pippali (<i>Piper longum</i>), Guggulu Shuddha (<i>Commiphora wightii</i>)</p>	<ul style="list-style-type: none"> • Anti-inflammatory (Shothanashak) • Anti-tumour (Gulmanashak) [4] • Triphala – Anti-cancer activity especially in breast cancer [16] • Guggulu – Anti-inflammatory, anti-oxidant and anti-cancer activity [17] • Pippali [12] – Anti-tumour activity [18]
5	<p>Liv-Atharva Liquid (LA)</p> <p>Kumari (<i>Aloe vera</i>), Haritaki (<i>Terminalia chebula</i>)</p>	<ul style="list-style-type: none"> • Liv-Atharva Liquid derived from classical Ayurvedic formulation Kumari Aasava, having hepato-protective, anti-tumour and digestive properties [5] • <i>Aloe vera</i> -Hepato-protective, immunomodulatory, anti-inflammatory and anti-tumorogenic activity; improves digestion and detoxifies various organs [12]; anti-cancer, anti-mitotic and specific protein inhibition [19] • Haritaki (<i>Terminalia chebula</i>) [12] – Digestive, laxative, Rasayana (immunomodulator)

6	<p>Pippalyadyasav (PLA)</p> <p>Draksha (Black raisins), Pippali (<i>Piper longum</i>)</p>	<ul style="list-style-type: none"> • Anti-tumour activity [5] • Draksha (Black raisins) [12]- Digestive, anti-inflammatory, hematinic, laxative, strengthening and beneficial in respiratory diseases. Anti-cancer, anti-inflammatory activity [20] • Pippali – Anti-tumour activity [18]
7	<p>Atharva Aloe Plus Tab</p> <p>Kumari (<i>Aloe vera</i>) Bhumyamalaki (<i>Phyllanthus niruri</i>) Haritaki (<i>Terminalia chebula</i>), Bibhitaki (<i>Terminalia bellirica</i>) Shunthi (<i>Zingiber officinale</i>), Maricha (<i>Piper nigrum</i>) Pippali (<i>Piper longum</i>) Sharpunkha (<i>Tephrosia purpurea</i>).</p>	<p>Improve appetite (Deepana), promote digestion (Pachana) and hepatoprotective (based on personal knowledge and practice)</p>
8	<p>Ostopix Tab</p> <p>Guduchi (<i>Tinospora cordifolia</i>) Amalaki (<i>Phyllanthus emblica</i>) Musta (<i>Cyperus rotundus</i>) Asthisrunkhala (<i>Cissus quadrangularis</i>)</p>	<ul style="list-style-type: none"> • <i>Cyperus scariosus</i> R. Br and <i>Cyperus rotundus</i> – Anti-oxidant and anti-inflammatory [21] • <i>Cissus quadrangularis</i> – Anti-oxidant, Anti-cancer and improving serum calcium and phosphorus levels and osteogenic activity [22,23]
9	<p>Kamdudha Vati (Mouktikyukta)</p> <p>Shankha Bhasma (Incinerated Conch) Shukti Bhasma (Incinerated Pearl shell) Kapardik Bhasma (Incinerated Cowrie) Mouktik Bhasma (Incinerated Pearl) Praval Bhasma (Incinerated Coral) Gairik Shuddha (Purified red ochre) Guduchi Satva (Starch preparation of herb – <i>Tinospora cordifolia</i>) Gum acacia (<i>Acacia arabica</i>)</p>	<ul style="list-style-type: none"> • Pitta pacifying action [13]
10	<p>Atharva Ananta Vati</p> <p>Ananta (<i>Cryptolepis buchanani</i> / <i>Decalepis hamiltonii</i>)</p>	<ul style="list-style-type: none"> • Pitta pacifying action [12] [13] • Anti-oxidant and hepato-protective activity [24]

11	<p>Prasham Vati</p> <p>Brahmi (<i>Bacopa monnieri</i>) Ashwagandha (<i>Withania somnifera</i>), Vacha (<i>Acorus calamus</i>) Pimpali moola (<i>Piper longum</i>) Parsic Yavani (<i>Hyascyamus niger</i>) Tagar (<i>Valeriana wallichii</i>) Shankhapushpi (<i>Convolvulus pluricaulis</i>)</p>	<ul style="list-style-type: none"> • Neuroprotective and stress relieving • Brahmi (<i>Bacopa monnieri</i>) - regulation of stress biomarker levels and support to brain to combat stressful conditions, improvement in antioxidant enzyme status, reduction in lipid peroxidation and tumor development markers; anti-oxidant and neuroprotective properties [25]
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Table 3: Adjunct Ayurvedic treatment with biological activities of ingredients and rationale behind selection of medicines.

ASBV, a herbo-mineral-metallic Rasayana (immunomodulator) was ascertained as a treatment of choice in all the sets of treatment for the entire period of 10 years 7 months in this metastatic TNBC patient. This was due to the fact that TNBC exhibits a higher rate of Tumour Infiltrating Lymphocytes (TIL) infiltration within the tumour environment, possibly as a result of somatic mutations that lead to emergence of neo-antigens and exacerbate the immune response. ASBV probably helped to prevent recurrence or distal metastasis, eliminated early and delayed toxicities of the 1st and 2nd line chemotherapeutic drugs, minimized general debility and helped to alleviate pulmonary disorders.

During the 1st set of Ayurvedic treatment (Table 1), this patient was additionally treated with Shatavari Kalpa, AV and TG. The anti-cancer activity of Shatavarins isolated from the roots of *Asparagus racemosus* (Wild) [14] and TG has been reported [16], while AV [3] was administered to this patient as a hepatoprotective drug of choice (Table 3). Elevated level of SGOT (44 U/l) at the time of enrolment due to hepatotoxic chemo-therapeutic medicines, Carboplatin and Paclitaxel as 2nd line chemotherapy, reduced to 26 U/l and later remained normal due to treatment with AV for long duration (Table 1) [15]. Effect of combination of AV and TG has also been reported to be hepatoprotective in non-alcoholic fatty liver disease [26].

In the 2nd set of Ayurvedic medicines (Table 1) the patient was treated with alcohol-based Ayurvedic formulations, viz., LA and PLA in place of AV and TG with the aim of having further improvement in liver and lung functions. LA and PLA are polyherbal drugs and the activity of each of the constituent herb is given in Table 3.

The 3rd set of Ayurvedic medicines (Table 1) was of the longest duration of Ayurvedic treatment, when the patient was treated with Tablet Aloe Plus and Ostopix Tab (Table 1) along with ASBV to increase the strength of bones because of two episodes of bone fractures. These medicines are also polyherbal in nature and the combination of these medicines was selected in view of risk of

TNBC to metastasize to liver and bones. The details of each herb are given in Table 3.

The 4th Set of Ayurvedic medicines (Table 1) consisted of MKD, Ananta Vati and Tab Prasham. Tab MKD and Ananta Vati having Pitta pacifying action [11] were administered due to the patient's symptoms of giddiness and vertigo. Tab Prasham was given in view of vascular malformation/ haemorrhagic venous infarcts in brain MRI (December 2020) and clinical symptoms of giddiness and neck stiffness during this period. It was also prescribed to prevent high incidence of brain metastasis leading to poor survival in TNBC patients [8].

The 5th set of Ayurvedic medicines (Table 1) comprising ASBV, LA and PLA beneficial in preventing respiratory diseases, was administered and still continued considering high risk of recurrence of lung metastasis or lung infection in SARS-CoV-2 pandemic scenario. This treatment was specifically beneficial to avoid aggressive lung infection in-spite of having SARS-CoV-2 infection in this patient.

Additional Ayurvedic treatment included specific procedures (Fig. 1) used in Panchakarma [27]. This modality of treatment is a total body detoxifying procedure, particularly to eliminate toxins deeply situated in all the tissues and organs, often adopted in Ayurvedic therapy with remarkable effect. These procedures are accompanied by oil-based treatment modalities, strict diet and lifestyle practices. Apart from Panchakarma, the patient was also treated with allied procedures such as Shirodhara and Shiropichu [28] and Pinda Sweda [29]. Shirodhara and Shiropichu are effective in stress management [30], which is considered as evident risk factor in TNBC. Pinda Sweda is a type of sudation in which a bolus of rice cooked with milk and herbal decoctions [29] is applied on the targeted part of the body such as chest region in this case.

Significant improvement in the Quality of Life and progression free survival have been reported in patients including TNBC patients undergoing yearly Panchakarma treatment.

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Reduction in inflammatory response based on serum cytokines, and ROS generation in erythrocytes extracts have also been studied in patients treated with Panchakarma [31]. Similarly, immunological and metabolic responses in a therapeutic course of Basti in obesity have documented modulation of immune responses by regulating pro-inflammatory cytokines, immunoglobulins and functional properties of T-cells, which are associated with a reduction in the body weight and its maintenance even after three months of treatment. [32]. Pharmacokinetic aspect of Lekhana Basti has also been analysed with the help of HPLC which suggests the absorption of phytochemicals from the Basti formulations in the systemic circulation [33].

Conclusion

In the present case of Stage IV (lung metastasis) TNBC with VUS mutation, the patient did not opt for any additional adjunct cancer therapy after starting Ayurvedic treatment. This patient belongs to high-grade, high-risk category with limited survival possibility. We, therefore, feel that the long progression free survival of 10 years 7 months with good quality of life, without adjunct cancer therapy could only be assigned to immunomodulatory, anti-inflammatory and anti-cancer effect of the herbo-mineral metallic oral medicines and periodic detoxifying Panchakarma treatment.

Acknowledgement

The authors wish to acknowledge the help of Ayurvedic physicians and Panchakarma Vaidya of Integrated Cancer Treatment and Research Centre, Wagholi, Pune in the treatment and follow up of patient.

Statement of Ethics

This case report has been written with the patient's consent.

Disclosure Statement

Part of the medicines used are under patent application numbers 201921018272; 17/609,535 and 202221023824.

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