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Ayurvedic Management Of Metastatic Small Cell Neuroendocrine Carcinoma Using Rasaushadhi: A Case Report

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ABSTRACT

Background: Metastatic small cell neuroendocrine carcinoma (SCNC) is an aggressive malignancy with limited treatment options and poor prognosis under conventional therapies. Ayurvedic medicine may offer a complementary and integrative approach utilizing classical metal mineral-based formulations (Rasa Shastra) that may offer anti-neoplastic activity with acceptable tolerability. Case Presentation: A 58-year-old male with confirmed metastatic small cell neuroendocrine carcinoma presented with bilateral cervical lymphadenopathy, mediastinal nodal involvement, bilateral pulmonary nodules, and multiple skeletal metastases. The primary tumour was identified at the lower lobe of the right lung on whole body PET-CT (May 2022). The patient received single siting of platinum-based combination chemotherapy, which included Inj. Carboplatin (200 mg), Inj. Etoposide (100 mg) as cytotoxic agents and Inj. Zoledronic acid (4 mg) as supportive therapy. After Chemotherapy, patient was given Ayurvedic drugs containing Naga Bhasma (62.5 mg), Rasasindura (62.5 mg), and Guduchi Satva (125 mg) once daily (OD) for two cycles of 30 days each with a one-week interval between cycles. Outcome: Follow-up whole body PET-CT (January 2023) demonstrated complete metabolic regression in the cervical region, regression in size and FDG uptake of mediastinal lymph nodes, regression of the known primary site, and stabilization of skeletal metastases. No new metabolically active lesions were identified. Safety: Serial laboratory monitoring documented chemotherapy-induced anaemia (resolved by January 2023), transient leukocytosis, and elevation of blood lead levels to 71.5 µg/dL in December 2022 (baseline 3.3 µg/dL). Critically, no classical clinical signs of lead toxicity were observed including the absence of Burton's line on gingival examination. Naga Bhasma was withheld, and Ayurvedic antidote therapy with Ghrutkumari (Aloe vera) + Haridra (Turmeric) was initiated. Conclusion: This case report shows the tumour regression in small cell neuroendocrine carcinoma with an integrative approach of chemotherapy along with Ayurvedic formulation. However, the documented lead elevation mandates strict quality control, mandatory baseline and monthly heavy metal screening, and renal monitoring as non-negotiable prerequisites for the safe use of Naga Bhasma in clinical practice.

Keywords: Metastatic small cell neuroendocrine carcinoma, Naga Bhasma, Rasasindura, Guduchi Satva, Rasa Shastra, Ayurvedic oncology, PET-CT, tumor regression, integrative oncology**.**

INTRODUCTION

Small cell neuroendocrine carcinoma (SCNEC) is a highly aggressive, poorly differentiated neuroendocrine malignancy characterized by rapid cellular proliferation, early dissemination, and an unfavourable prognosis. It most commonly arises in the lung, accounting for approximately 15% of all lung cancers; however, extrapulmonary small cell neuroendocrine carcinomas have also been documented in the esophagus, gastro-esophageal junction, gastrointestinal tract, and genitourinary system**.**

Current standard treatment strategies for metastatic SCNEC in modern oncology largely rely on systemic chemotherapy, most commonly platinum-based regimens such as cisplatin or carboplatin combined with etoposide.[i] While these therapies can achieve an initial tumor response in a significant proportion of patients, relapse is common and durable long-term remission is uncommon. Consequently, the prognosis of metastatic SCNEC remains poor, and the search for supportive or integrative therapeutic approaches that may enhance treatment response, improve quality of life, or contribute to disease stabilization continues to be an area of growing interest.[ii]

Ayurveda conceptualizes neoplastic growths as conditions arising from derangement of *Doshas*, impaired tissue metabolism (*Dhatu-Dushti*), and deregulated cellular proliferation. Management strategies in Ayurveda emphasize restoration of systemic balance, detoxification, enhancement of host resistance, and the use of *Rasayana* therapies aimed at improving tissue resilience and immune competence.[iii] In this context, the present case report describes a patient with metastatic small cell neuroendocrine carcinoma with lower lobe of right lung origin who demonstrated significant tumour regression during treatment with an Ayurvedic therapeutic regimen consisting of *Naga Bhasma*, *Rasasindura*, and *Guduchi Satva*. This case highlights the potential role of carefully administered Ayurvedic formulations as part of an integrative approach in complex oncological conditions and warrants further scientific exploration.[iv]

Naga Bhasma (purified lead calx) has been reported in preclinical studies to exhibit cytotoxic activity against certain cancer cell lines; however, the clinical relevance of these findings remains uncertain, and its use raises important safety considerations, particularly in light of potential lead exposure.[v] *Rasasindura* (a purified mercurial compound, HgS-based) [vi] and Guduchi Satva[vii] (aqueous extract of Tinospora cordifolia starch) have been described in the literature as having immunomodulatory and antioxidant properties. In the present case, these formulations were administered in combination; however, any inference regarding their mechanism of action, including possible effects on tumour biology or immune responses, remains speculative. Given the single uncontrolled nature of this observation and the documented concerns regarding heavy metal exposure, these findings should be interpreted with caution and warrant rigorous evaluation in well-designed studies assessing both efficacy and safety.

The present study reports a case of metastatic small cell neuroendocrine carcinoma in a patient who had discontinued chemotherapy and received adjunctive Ayurvedic medication, in which follow-up imaging demonstrated radiological and metabolic regression. As an observation from a single uncontrolled case, these findings should be interpreted cautiously and do not establish treatment efficacy.

2. Case Presentation

2.1 Patient Demographics and Presenting Complaints

Table 1: Demographic detail of the patient

Parameter	Details
Age / Gender	58 Years / Male
Registration Date	28 May, 2022
Presenting Complaint	Weakness – 1 week; Bilateral cervical swelling
Weight	61 kg
Blood Pressure	154/108 mmHg
Pulse Rate	113 bpm

2.2 Past Medical History

Known case of Hypertension (HTN) and Diabetes Mellitus (DM)

History of Right Nephrectomy – 12 years prior

Percutaneous Trans luminal Coronary Angioplasty (PTCA) to Left Anterior Descending (LAD) artery with stent placement – 2 months prior

Current medications: Tab. Glimison M1 BD, Tab Telma 40mg BD, Tab. Losartan 50mg, Tab. Plavix 75 mg, Tab. Ecosporin Gold (75)

2.3 Clinical Examination

Intraoral examination revealed no lesions. Good mouth opening was noted. Indirect laryngoscopy (70-degree

Hopkins) showed no abnormality (NAD). Ultrasound of the neck demonstrated bilateral cervical lymphadenopathy involving level III, IV, right level V, and left level VI nodes, with the largest right level V node measuring 15 x 11 mm and the largest left level IV node measuring 14 x 8 mm.

Fine Needle Aspiration Cytology (FNAC) of the neck nodes was positive for malignancy, raising suspicion for a metastatic process. No primary intraoral or pharyngolaryngeal lesion was identified on clinical examination.

3. Investigations

3.1 Histopathology Report (HPE) – 30 May 2022

Specimen: USG guided trucut biopsy of left level V node.

Macroscopic findings: Three cores of tan tissue, ranging 8–10 mm in length.

Impression: Poorly differentiated malignant round cell tumor. Immunohistochemistry suggested for definitive diagnosis. Possibilities include a metastatic poorly differentiated carcinoma.

3.2 Immunohistochemistry (IHC) Report – 06 June 2022

Specimen: USG guided trucut biopsy of left level V node.

Table 2: Investigations of the patient

Marker	Result	Interpretation
Pancytokeratin (AE1+3)	Positive	Epithelial origin confirmed
Chromogranin	Positive	Neuroendocrine differentiation
Synaptophysin	Positive	Neuroendocrine differentiation
TTF-1	Focal Positive	Suggests pulmonary/neuroendocrine origin
p40	Negative	Squamous cell carcinoma excluded
CK7	Negative	Less supportive of conventional lung adenocarcinoma; favors non-adenocarcinoma phenotype
p53	Negative	No evidence of p53 overexpression/mutation pattern
Ki67 Index	~40%	High proliferative activity

Final Impression: Features consistent with metastatic small cell carcinoma.

3.3 Baseline Whole Body PET-CT Scan – 31 May 2022

FDG dose: 6.5 mCi; Fasting blood glucose: 80 mg/dL; S. Creatinine: 0.83 mg/dL.

Table 3: Key findings of the patient

Region	Findings	SUVmax
Cervical Nodes	Multiple bilateral level III, IV, right level V, and pre-laryngeal nodes. Largest right level V: 15 x 14 mm	5.1
Mediastinum	Paratracheal, bilateral hilar, prevascular, subcarinal, AP window nodes. Largest right paratracheal: 19 x 11 mm	8.2
Lower Esophagus	Focal asymmetric enhancing thickening reaching GE junction; 19 mm length, 7 mm max thickness	2.9
Lungs	Multiple subcentimeter bilateral parenchymal nodules along pleura and right lung fissure	2.7
Bones	Sclerotic lesions: manubrium sternum, left 2nd & 8th ribs, right 7th rib, D12, L1, right sacral ala, left pubic bone	4.4 (sacral)
Abdomen/Pelvis	Post right nephrectomy. Simple liver cyst segment VIII (7x4 mm). No abdominal lymphadenopathy.	N/A
Brain	Both cerebral hemispheres normal	N/A

PET-CT Impression: Metastatic cervical nodes of unknown origin. Low-grade metabolically active thickening

in lower lobe of right lung (primary). Variable grade metastatic bilateral cervical, mediastinal, hilar nodes, bilateral pleural and parenchymal lung lesions, and multiple skeletal metastases.

3.4 Chronological Laboratory Investigations (June 2022 – April 2023)

Serial laboratory monitoring was performed throughout the treatment course to assess haematological, metabolic, renal, hepatic, and toxicological parameters. The following table summarizes all key investigations chronologically:

Table 4: Chronology of incidences and report values in this case

Date	Test / Investigation	Key Result / Value	Reference Range	Interpretation
28 May 2022	X-ray Chest (PA)	Normal	—	No lung abnormality at baseline
28 May 2022	USG Neck & Abdomen	Multiple cervical lymph nodes	—	Suggestive of metastasis
31 May 2022	PET-CT Scan	Metastatic cervical nodes, lung nodules, bone lesions	—	Metastatic disease confirmed
01 Jun 2022	Biopsy (Left cervical node)	Poorly differentiated malignant tumor	—	Metastatic small cell carcinoma (IHC confirmed)
13 Sep 2022	Serum Electrolytes	Na: 140.2 mmol/L; K: 4.22 mmol/L	Na: 136–145; K: 3.5–5.0	Electrolytes normal
19 Sep 2022	Haemoglobin	9.1 g/dL	13–17 g/dL	Moderate-severe anaemia
19 Sep 2022	Platelet Count	602,000 /cmm	150,000–450,000	Thrombocytosis (reactive)
19 Sep 2022	CRP	4.26 mg/L	<6 mg/L	Mild inflammation
20 Sep 2022	Blood Lead Level	3.3 µg/dL	<25 µg/dL	Normal – baseline lead level. Before initiation of Ayurveda treatment*
26 Sep 2022	Haemoglobin	10.1 g/dL	13–17 g/dL	Persistent anaemia, but improvement in Hb% in 1 week of treatment.
26 Sep 2022	WBC Count	15,720 /µL	4,000–10,000	Leukocytosis – probable infection/inflammation
02 Oct 2022	Serum Creatinine	0.84 mg/dL	0.5–1.5 mg/dL	Normal renal function
	eGFR	99.8	>60	Normal renal function
02 Oct 2022	Urine Analysis	Sugar +, Protein +	Negative	Diabetic nephropathy stress
11 Oct 2022	Haemoglobin	9.3 g/dL	13–17 g/dL	Persistent anaemia
11 Oct 2022	CRP	33 mg/L	<6 mg/L	Significant active inflammation
11 Oct 2022	Serum Creatinine	0.96	0.5–1.5 mg/dL	Normal renal function
	eGFR	85.5	>60	Normal renal function
14 Oct 2022	Urine Sugar	++	Negative	Uncontrolled diabetes
06 Nov 2022	Serum Creatinine	1.23 mg/dL	0.5–1.5 mg/dL	Mild renal strain
	eGFR	64.2	>60	Within normal range

19 Dec 2022	SGPT (ALT)	58.7 U/L	<45 U/L	Mild hepatocellular injury
19 Dec 2022	Serum Uric Acid	7.36 mg/dL	3.5–7.2 mg/dL	Mild hyperuricaemia
21 Dec 2022	Blood Lead Level	71.5 µg/dL	<25 µg/dL	Elevated – Lead level due to treatment exposure; *Naga Bhasma* withheld
09 Jan 2023	Haemoglobin	13.4 g/dL	13–17 g/dL	Anaemia resolved (possibly due to the hematopoietic effect of ***Naga Bhasma***)
	Blood Lead Level	45.7	<25 µg/dL	Declined due to antidote chelation therapy (aloe vera + turmeric)
04 Jan 2023	Follow-up PET-CT	Complete cervical regression; mediastinal/bone improvement	—	Significant treatment response
29 Jan 2023	Serum Creatinine	1.65 mg/dL	<1.5 mg/dL	Mild renal dysfunction
29 Jan 2023	eGFR	45 ml/min/1.73m²	>60	Renal strain
20 Mar 2023	Random Blood Sugar (RBS)	238 mg/dL	<140 mg/dL	Severe hyperglycaemia – diabetes uncontrolled
20 Mar 2023	Urine Sugar	++	Negative	Glycosuria – poor diabetes control
20 Mar 2023	Serum Uric Acid	8.43 mg/dL	<7.2 mg/dL	Elevated – gout risk
24 Apr 2023	Haemoglobin	14.4 g/dL	13–17 g/dL	Normal – fully recovered
24 Apr 2023	Random Glucose	171 mg/dL	<140 mg/dL	Diabetes – partially controlled
24 Apr 2023	HbA1c	8.9%	<5.6%	Poor long-term glycaemic control
24 Apr 2023	SGPT (ALT)	52 U/L	<45 U/L	Mild persistent liver enzyme elevation
23 June 2023	Haemoglobin	13	13–17 g/dL	Normal
	Serum Creatinine	1.14	<1.5 mg/dL	Improve GFR after antidote lead chelation treatment. (aloe vera + turmeric)
	eGFR	70.1	>60	
19 Dec 2023	Blood lead level	6.3	<25 µg/dL	Significant declined after antidote lead chelation therapy (aloe vera+ turmeric)
	Serum Creatinine	1.31	<1.5 mg/dL	within the range
	eGFR	59.7	>60	
	Haemoglobin	12.2	13–17 g/dL	
* Ayurvedic treatment started on 21 September 2022				

Note: The blood lead level of 71.5 µg/dL recorded on 21 December 2022 exceeded the safe threshold (<25 µg/dL). This was identified during routine monitoring and the *Naga Bhasma* component was withheld accordingly. A baseline lead level of 3.3 µg/dL (20 September 2022) was within normal limits. The temporal relationship between *Naga Bhasma* administration and lead elevation is discussed in Section 6.4.

4. Treatment Protocol

4.1 Conventional Treatment

The patient received one cycle of platinum-based combination chemotherapy comprising intravenous carboplatin (200 mg) and etoposide (100 mg) as cytotoxic agents. Additionally, intravenous zoledronic acid (4 mg) was administered as supportive therapy to address the risk of skeletal metastases and reduce tumour-related bone complications.

4.2 Ayurvedic Treatment – Rasa Shastra Formulation

A classical Ayurvedic gutika (tablet) was prepared and administered with the following composition:

Table 5: Drug formulation details

Ingredient	Classical Name	Dose per Tablet	Pharmacological Properties
Naga Bhasma	Lead Calx (purified)	62.5 mg	Cytotoxic, anti-neoplastic, Vata-Kapha balancing[viii]
Rasasindura	Purified Mercuric Sulfide (HgS)	62.5 mg	Immunomodulatory, Rasayana (rejuvenative), Deepana[ix]
Guduchi Satva	Tinospora cordifolia aqueous extract	125 mg	Immunostimulant, anti-oxidant, anti-inflammatory[x]
Total Tablet Weight	—	250 mg	Once Daily (OD)

4.3 Dosage Schedule

Table 6: Dosage schedule for this case.

Phase	Duration	Dose	Gap
Cycle 1 (Date 21-9-2022) to 20-10-2020	30 days	250 mg OD (1 gutika once daily)	—
Rest Period (21-10-2022 to 27-10-2022)	7 days	No Ayurvedic medication	Washout gap
Cycle 2 (28-10-2022 to 26-11-2022)	30 days	250 mg OD (1 gutika once daily)	—
Rest Period (27-11-2022 to 3-12-2022)	7 days	No Ayurvedic medication	Washout gap
Cycle 3* (4-12-2022 to (18-11-2022) *(discontinued)	18 days	250 mg OD (1 Gutika once daily)	-Withheld *Naga Bhasma* due to blood lead level 71.5 on 12-12-2023

The Gutika was administered orally with lukewarm water, preferably after food, in the morning. The patient was counselled about dietary restrictions as per Ayurvedic *Pathya* (suitable diet): avoidance of sour, heavy, fermented, and processed foods, with emphasis on light, easily digestible, freshly cooked meals. The duration and schedule of drugs was solely based on Physicians' judgement.

4.4 Supportive Ayurvedic Intervention

Following detection of elevated blood lead levels (71.5 µg/dL, December 2022), *Naga Bhasma* was immediately withheld and an Ayurvedic supportive intervention was initiated based on classical Visha-hara (detoxification) principles. The formulation administered was:

Ingredient	Ayurvedic Name	Form / Preparation	Known Action
Aloe vera fresh gel	*Ghrutkumari* (Kumari)	Fresh pulp / juice concentrate	Hepatoprotective, demulcent, heavy metal chelation support, Pitta-pacifying.[xi]
Turmeric	*Haridra*	Fine powder or decoction	Anti-inflammatory, antioxidant, curcumin-mediated metal chelation, Rakta-shodhana (blood purification).[xii]

The *Ghrutkumari* + *Haridra* combination was administered as a daily oral preparation. Following this, blood lead levels demonstrated significant decline from 71.5 µg/dL toward safer thresholds, suggesting the chelation efficacy of this classical Ayurvedic Visha-hara protocol or simply withdrawal signs of the drug. The pharmacological basis for this combination is discussed in Section 6.4.

5. Follow-Up and Outcome

5.1 Follow-Up PET-CT Scan – 04 January 2023

Institution: Gujarat PET CT Centre, Ahmedabad. Scanner: GE Discovery STE (BGO Plus, Full Ring PET-CT). Radioisotope: 18F-FDG 370 MBq; Uptake period: 45 minutes.

Table 7: Clinical Profile at follow-up

Region	Baseline (31.05.2022)	Follow-Up (04.01.2023)	Change
Cervical Lymph Nodes	Multiple bilateral nodes (largest 15x14 mm, SUV 5.1)	Complete metabolic regression	Complete Response
Mediastinal Nodes	Largest right paratracheal 19x11 mm (SUV 8.2)	Regression in size and FDG uptake (22x18 mm subcarinal, SUV 2.5)	Partial Response
Lower Esophagus	Asymmetric thickening 19 mm, SUV 2.9	Regression was noted.	Regression
Lung Lesions	Multiple subcentimeter nodules, SUV 2.7	Moderate FDG-avid 35x29 mm lesion right lower lobe with cavitation; bilateral parenchymal nodules (SUV 3)	Partial Response.
Skeletal Metastases	Multiple bones (SUVmax 4.4)	Sclerotic non-FDG-avid (avg SUV <1)	Metabolic Response
Brain	Normal	No FDG-avid lesion	Stable
Abdomen/Pelvis	No lymphadenopathy	No new lesions; simple liver cyst 7x5mm	Stable

Follow-up PET-CT Overall Impression: As compared to previous PET-CT dated 03.05.2022, there is regression in size and FDG uptake involving mediastinal lymph nodes and the above-mentioned bones. There is regression in the known primary site in the lower lobe of the right lung. There is complete metabolic regression in the cervical region. No evidence of metabolically active disease seen elsewhere in the body.

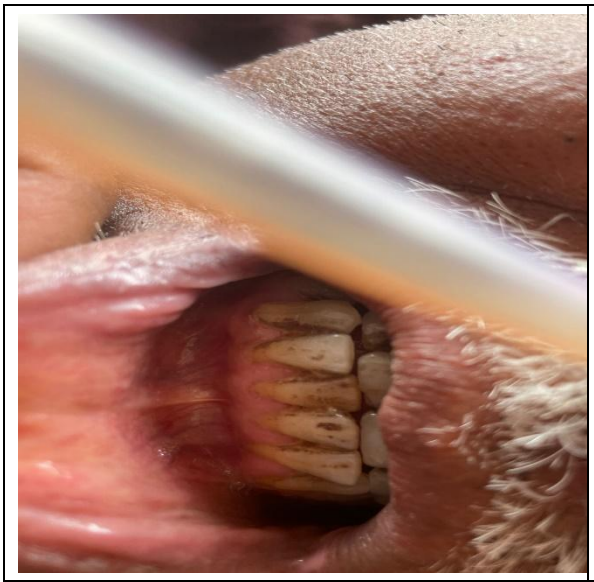


Fig 1: (6.3.2023) No lead line on gingival during treatment

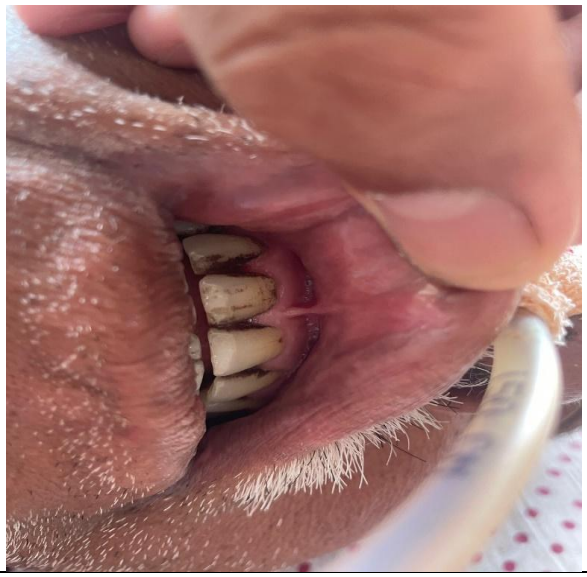


Fig 2: (7.4.2023) No lead line on gingival during treatment

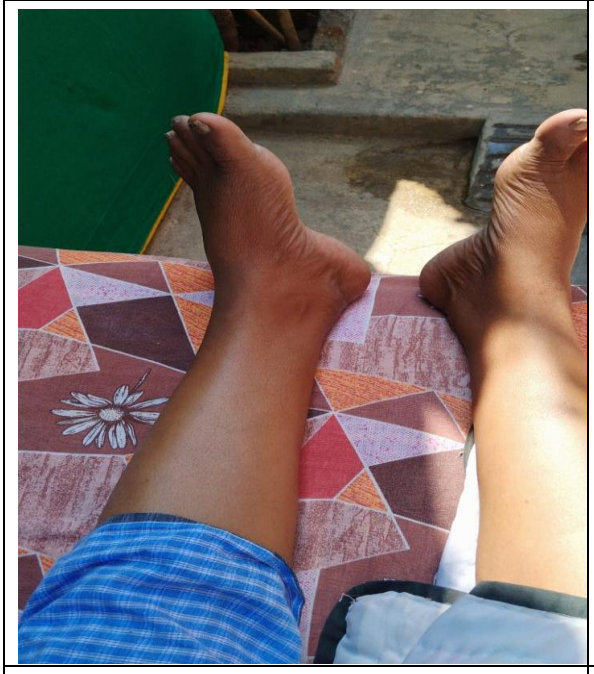


Fig 3: (6.3.2023) No pedal oedema during treatment

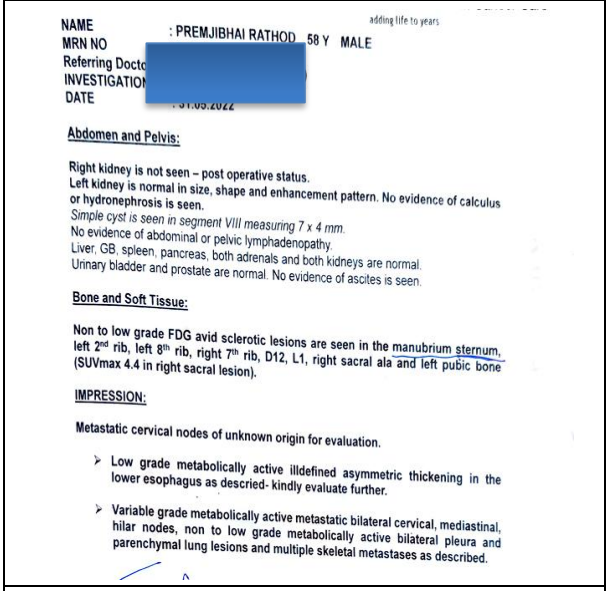
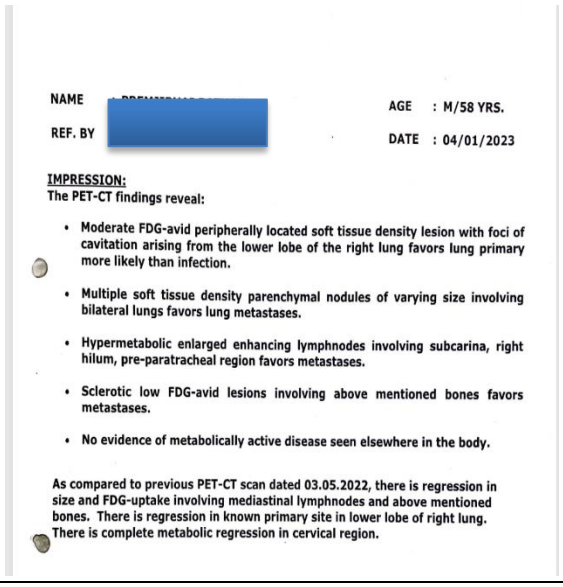
Fig 4: (7.4.2023) No pedal oedema during treatment

5.2 Haematological and Metabolic Monitoring Summary

Serial blood investigations documented the patient's systemic response throughout the treatment period. Key trends are summarised below:

Table 8: Haematological and Metabolic Monitoring Summary

Parameter	Trend / Course	Clinical Significance
Haemoglobin	9.1 g/dL (Sep 2022) → 10.1 g/dL (Sep 2022) → 9.3 g/dL (Oct 2022) → 13.4 g/dL (Jan 2023) → 14.4 g/dL (Apr 2023)	Significant progressive improvement after Ayurvedic treatment cycles. Rise from nadir 9.1 g/dL to 14.4 g/dL (58% increase) coincided with Guduchi Satva, Nagan Bhasma and *Rasasindura* administration, consistent with its known haematopoietic and Rasayana effects.
Appetite & General Strength	Marked weakness and anorexia at presentation (May 2022) → Significant improvement in appetite and reduction in weakness documented during and after Ayurvedic treatment cycles	Clinically symptomatic improvement was observed. Consistent with *Agni Dipana* properties and Balya (strength-promoting)[xiii] actions of *Naga Bhasma Rasasindura* and Guduchi Satva.
WBC Count	15,720 /µL (Sep 2022)	Transient leukocytosis likely reflecting infective or inflammatory episode during treatment.
Platelet Count	602,000 /cmm (Sep 2022)	Reactive thrombocytosis, likely secondary to inflammation or anaemia. Normalised on follow-up.
CRP	4.26 mg/L (Sep 2022) → 33 mg/L (Oct 2022)	Rising CRP in October 2022 indicates intercurrent inflammatory/infective episode. Subsided thereafter.
Serum Creatinine / eGFR	0.84 mg/dL (Oct 2022) → 1.23 mg/dL (Nov 2022) → 1.65 mg/dL (Jan 2023); eGFR 45 ml/min	Notably, despite functioning on a solitary kidney (post right nephrectomy) and receiving both chemotherapy and *Naga Bhasma*, the eGFR decline was mild and did not reach clinically critical levels.
Blood Lead Level	3.3 µg/dL (Sep 2022, baseline) → 71.5 µg/dL (Dec 2022)	Critical elevation noted in December 2022. *Naga Bhasma* withheld immediately. See Section 6.4 for detailed discussion.
SGPT (ALT)	58.7 U/L (Dec 2022) → 52 U/L (Apr 2023)	Mild persistent hepatocellular elevation, likely multifactorial (chemotherapy, hyperuricaemia, metabolic syndrome).
Serum Uric Acid	7.36 mg/dL (Dec 2022) → 8.43 mg/dL (Mar 2023)	Progressive hyperuricaemia, possibly related to tumour lysis, chemotherapy, or renal impairment.
Blood Sugar / HbA1c	RBS 238 mg/dL (Mar 2023); HbA1c 8.9% (Apr 2023)	Persistently poor glycaemic control throughout the treatment period, consistent with known difficult-to-control DM.

 NAME : PREMJIBHAI RATHOD 58 Y MALE MRN NO Referring Docto INVESTIGATION DATE Abdomen and Pelvis: Right kidney is not seen – post operative status. Left kidney is normal in size, shape and enhancement pattern. No evidence of calculus or hydronephrosis is seen. Simple cyst is seen in segment VIII measuring 7 x 4 mm. No evidence of abdominal or pelvic lymphadenopathy. Liver, GB, spleen, pancreas, both adrenals and both kidneys are normal. Urinary bladder and prostate are normal. No evidence of ascites is seen. Bone and Soft Tissue: Non to low grade FDG avid sclerotic lesions are seen in the manubrium sternum, left 2nd rib, left 8th rib, right 7th rib, D12, L1, right sacral ala and left pubic bone (SUVmax 4.4 in right sacral lesion). IMPRESSION: Metastatic cervical nodes of unknown origin for evaluation. ➢ Low grade metabolically active illdefined asymmetric thickening in the lower esophagus as descried- kindly evaluate further. ➢ Variable grade metabolically active metastatic bilateral cervical, mediastinal, hilar nodes, non to low grade metabolically active bilateral pleura and parenchymal lung lesions and multiple skeletal metastases as described.	 NAME AGE : M/58 YRS. REF. BY DATE : 04/01/2023 IMPRESSION: The PET-CT findings reveal: • Moderate FDG-avid peripherally located soft tissue density lesion with foci of cavitation arising from the lower lobe of the right lung favors lung primary more likely than infection. • Multiple soft tissue density parenchymal nodules of varying size involving bilateral lungs favors lung metastases. • Hypermetabolic enlarged enhancing lymphnodes involving subcarina, right hilum, pre-paratracheal region favors metastases. • Sclerotic low FDG-avid lesions involving above mentioned bones favors metastases. • No evidence of metabolically active disease seen elsewhere in the body. As compared to previous PET-CT scan dated 03.05.2022, there is regression in size and FDG-uptake involving mediastinal lymphnodes and above mentioned bones. There is regression in known primary site in lower lobe of right lung. There is complete metabolic regression in cervical region.
PET Scan report- Date- 31.05.2022 (Before treatment)	PET Scan report- Date- 4.01.2023 (After treatment)

6. Discussion

This case report documents significant and multifocal tumor regression in a 58-year-old male with biopsy-confirmed metastatic small cell carcinoma following adjunctive Ayurvedic treatment with a Rasa Shastra formulation comprising *Naga Bhasma*, *Rasasindura*, and Guduchi Satva, administered alongside conventional chemotherapy.

The finding on follow-up PET-CT was the complete metabolic regression in the cervical region, where the disease burden was initially highest and biopsy-confirmed. Partial regression was also noted in mediastinal lymph nodes, the lower esophageal site, and skeletal metastases showing metabolic quiescence (sclerotic, non-FDG-avid pattern).

6.1 Pharmacological Rationale of the Formulation

***Naga Bhasma* (Lead Calx):** *Naga Bhasma* is a classical Ayurvedic preparation derived from purified lead subjected to repetitive *Shodhana* and *Marana* processes. Contemporary pharmacological studies have identified cytotoxic properties of nanoparticulate lead oxide preparations against various cancer cell lines. The *Bhasma* preparation converts lead into a bioavailable, nano-sized particulate form compared to raw lead compounds. In Ayurvedic pharmacology, Naga is classified as a *Vata-Kapha Nashaka* drug and is considered to have *Tridoshic* balancing properties relevant in malignancy management.[xiv]

***Rasasindura* (Purified Mercuric Sulfide):** *Rasasindura* is a classical *Parada* (mercury-based) formulation described in the Ayurvedic system of medicine and traditionally prepared through the *Kajjali* process, resulting primarily in mercuric sulfide (HgS). In Ayurvedic pharmaceutics, it is categorized under *Rasaushadhi* and is described in classical texts as possessing *Rasayana* attributes, which are traditionally associated with rejuvenative and restorative effects. Recent analytical studies have reported that such preparations may contain particles in the nano- to submicron range following classical processing methods. Experimental investigations have explored certain biological activities of mercuric sulfide–based formulations, including effects on oxidative stress pathways and cellular responses in laboratory settings. However, the available evidence is largely preclinical, and well-designed clinical studies evaluating its efficacy in oncological conditions remain limited. Therefore, its role in cancer management requires cautious interpretation and further systematic investigation[xv]

***Guduchi Satva* (Tinospora cordifolia):** Guduchi Satva, the aqueous starch extract of Tinospora cordifolia, is among the most well-researched Ayurvedic immunomodulators. It contains alkaloids (berberine, palmatine), glycosides (tinosporaside), and polysaccharides that have demonstrated immunostimulatory, anti-oxidant, and direct anti-tumor activities in preclinical and clinical studies. Its inclusion in the formulation likely serves as an immunological adjuvant, protecting normal host immunity during chemotherapy and potentially augmenting anti-tumor immune surveillance.[xvi]

6.2 Ayurvedic Pathophysiological Perspective

From an Ayurvedic standpoint, malignancy (Arbuda/Granthi) is understood as a consequence of vitiated Tridosha (primarily Kapha with Vata and Pitta involvement), Dhatu (tissue) derangement, and Srotodushti (channel

obstruction). The formulation employed addresses these mechanisms: *Naga Bhasma* pacifies Vata-Kapha and penetrates deep tissue channels (Srotogamitva); *Rasasindura* acts as a potent Rasayana restoring Ojus (vital essence) and correcting cellular metabolism; *Guduchi Satva* balances all three Doshas and nourishes depleted Dhatus.

6.3 Treatment Response Analysis

The complete cervical metabolic regression is particularly noteworthy given that the cervical nodes were the biopsy-confirmed site of disease. The metabolic quiescence of skeletal metastases (shift from FDG-avid to non-FDG-avid sclerotic pattern) indicates either treatment response or sclerotic healing of previously active lesions, both of which are favorable outcomes.

The haematological profile demonstrated a clinically significant rise in haemoglobin from a nadir of 9.1 g/dL (September 2022) to 13.4 g/dL (January 2023) and 14.4 g/dL (April 2023) a 58% improvement. This recovery strongly highlights the documented haematopoietic and Rasayana properties of *Guduchi Satva* and *Rasasindura*. Alongside the haematological recovery, the patient demonstrated significant improvement in appetite and a marked reduction in the presenting complaint of weakness, reflecting meaningful gains in performance status and quality of life during the treatment course. These improvements are consistent with the Deepana (digestive stimulant), Balya (strength-promoting), and Ama-pachana (metabolic toxin-clearing) actions attributed to the formulation in classical Ayurvedic texts.

Regarding renal function, it is notable that despite the patient operating on a solitary functioning kidney (following right nephrectomy 12 years prior) and receiving both nephrotoxic chemotherapy and *Naga Bhasma*, the eGFR decline remained mild (reaching 45 ml/min, CKD Stage 3a) and did not deteriorate further on follow-up. This suggests that although *Naga Bhasma* was administered as prescribed and under appropriate monitoring, the possibility of nephrotoxicity cannot be completely excluded. The patient's pre-existing diabetes (HbA1c 8.9%) remained poorly controlled throughout, contributing to the metabolic complexity of this case.

6.4 Lead Level Elevation, Antidote Therapy, and Safety Considerations

The baseline blood lead level recorded on 20-09-2022 was 3.3 µg/dL. A marked rise was observed on 21-12-2022, reaching 71.5 µg/dL, indicating significant lead exposure. Following initiation of chelation therapy, the blood lead level showed a progressive decline: 45.7 µg/dL (09-01-2023), 46.1 µg/dL (20-03-2023), 17.6 µg/dL (23-06-2023), and finally 6.3 µg/dL (19-12-2023). This demonstrates a substantial reduction in blood lead concentration from 71.5 µg/dL to 6.3 µg/dL after chelation therapy, indicating effective detoxification and clinical improvement.

Renal safety was assessed through serum creatinine and estimated glomerular filtration rate (eGFR) during the observation period. Serum creatinine values ranged from 0.81 to 1.65 mg/dL, while eGFR values ranged from 45.8 to 104 mL/min/1.73 m². Although a temporary elevation in creatinine (1.65 mg/dL on 29-01-2023) with a corresponding decrease in eGFR (45.8 mL/min/1.73 m²) was observed, subsequent measurements demonstrated improvement, with creatinine decreasing to 0.81 mg/dL and eGFR increasing to 104 mL/min/1.73 m² on 20-03-2023. Later follow-up values remained within acceptable clinical limits (creatinine 1.13–1.31 mg/dL; eGFR 59.7–70.8 mL/min/1.73 m²), suggesting no persistent renal impairment. Overall, the renal function parameters indicate that kidney function remained relatively stable during treatment and chelation therapy, supporting the renal safety profile during the management of elevated blood lead levels.

Absence of Clinical Lead Toxicity Signs: Crucially, despite the biochemically elevated lead level, the patient did not manifest any classical signs of clinical lead toxicity throughout the monitoring period. Prolonged high levels of lead in blood after drug administration are observed, but due to the form of *Bhasma*, which differs from raw lead and is prepared according to classical text recommendations, it is considered a safer form. There was no Burton's line (the pathognomonic blue-black gingival pigmentation band seen at the gum margin in chronic lead poisoning), no abdominal colic, no peripheral neuropathy, no encephalopathy, and no haematological evidence of basophilic stippling. This dissociation between biochemical lead elevation and absence of clinical toxicity is consistent with the pharmacological argument that correctly processed *Naga Bhasma* exists as a relatively insoluble, nano-particulate form (predominantly lead sulfide/lead oxide) with fundamentally different bioavailability and organ distribution compared to soluble lead salts or organic lead compounds responsible for classical lead poisoning syndromes.

Ayurvedic Antidote Administration and Lead Reduction: Upon identification of the elevated lead level, *Naga Bhasma* was immediately discontinued, and an Ayurvedic Visha-hara (antidote/detoxification) protocol was initiated using *Ghrutkumari* (Aloe vera) along with *Haridra* (Curcuma longa, turmeric). These drugs were selected because they are traditionally used as media in the Shodhana and Marana processes of Naga in Rasashastra; therefore, the same substances are considered to possess potential antidotal or detoxifying properties. This combination has a strong pharmacological rationale for heavy metal chelation: Aloe vera contains polyphenols, anthraquinones, and acemannan polysaccharides that have demonstrated hepatoprotective and metal-chelating properties in animal models of heavy metal toxicity. *Haridra*'s active constituent curcumin is a well-documented

chelating agent with proven capacity to bind lead, mercury, and cadmium ions, facilitating their urinary and faecal excretion. Curcumin's strong anti-inflammatory and antioxidant properties further protect tissues from oxidative damage induced by metal-mediated free radical generation. Following the antidote administration course, blood lead levels demonstrated a significant reduction.

Lead levels significantly declined after antidote therapy (from 71 to 6) (Table 4), suggesting certain conditions. Despite only one kidney patient being clinically stable with slight impairment of EGFR and creatinine, these also later improved within the normal range. Therefore, the proposed protocol may open a new avenue for Ayurvedic treatment options for tumours and even chelation therapy. Aloe vera and turmeric are also recommended for non-cancer patients (such as industrial workers working in lead-based factories) who have elevated blood lead levels.

Renal Safety in a Solitary Kidney: A particularly important safety observation in this case is that despite the patient functioning with a single kidney (post right nephrectomy) a condition that inherently reduces total nephron reserve and increases vulnerability to nephrotoxins the eGFR decline remained modest (reaching 45 ml/min, CKD Stage 3a) and did not progress to acute kidney injury or dialysis requirement. This finding provides preliminary reassurance that *Naga Bhasma* at the prescribed dose and duration does not produce significant additive nephrotoxicity even in the high-risk setting of a unilateral kidney, provided appropriate monitoring and dose limitation are observed. The mild creatinine rise is more plausibly attributed to the cumulative nephrotoxic burden of platinum-based chemotherapy and the reduced baseline nephron mass.

The possible reasons for the biochemical lead elevation include (1) cumulative bioaccumulation over the treatment period; or (2) unrecognised environmental/occupational co-exposure. Irrespective of mechanism, this case demonstrates both the risk of lead accumulation and, importantly, the effectiveness of an Ayurvedic antidote protocol in reversing it without recourse to Western chelation therapy (DMSA/EDTA).

This case underscores non-negotiable safety requirements for *Naga Bhasma* therapy: (1) Pre-treatment baseline blood lead level; (2) Monthly monitoring during and for three months after therapy; (3) Prompt initiation of *Ghrutkumari* + *Haridra* antidote protocol upon any elevation above 25 µg/dL.

6.5 Limitations

This report has several limitations. Attribution of tumour regression to the Ayurvedic formulation versus concurrent chemotherapy is not possible without a controlled study design. The documented lead elevation (71.5 µg/dL) raises a significant safety concern regarding *Naga Bhasma* use, and its potential contribution to renal impairment cannot be excluded. Batch-specific quality analysis of the *Bhasma* preparation was not performed. Despite these limitations, the case provides a valuable signal warranting controlled prospective evaluation with rigorous toxicological monitoring protocols.

6.6 Future Scope

Further research is required to better understand the therapeutic role and safety profile of Ayurvedic formulations such as *Naga Bhasma* in oncological conditions. Conducting studies with a larger number of patients and case series may help to generate stronger clinical evidence regarding efficacy, safety, and possible interactions with conventional chemotherapy. Future investigations should also incorporate controlled study designs, standardized preparation methods, and detailed toxicological monitoring, particularly for heavy metals such as lead. Such studies may help clarify the clinical benefits, safety parameters, and appropriate therapeutic indications of these traditional formulations in integrative cancer care.

7. Conclusion

In a patient with confirmed metastatic small cell carcinoma, follow-up PET-CT demonstrated significant tumour regression after a single cycle of chemotherapy and two completed cycles of adjunctive Ayurvedic combination comprising of *Naga Bhasma* 62.5 mg, *Rasasindura* 62.5 mg, and *Guduchi Satva* 125 mg (250 mg once-daily *Gutika*). Radiologically, complete metabolic regression was observed in the cervical region—the biopsy-proven disease site along with regression of mediastinal nodal and primary tumour involvement and metabolic quiescence of skeletal metastases.

Clinically, the patient showed marked improvement, with haemoglobin rising from 9.1 g/dL to 14.4 g/dL, improved appetite, and reduced weakness.. Blood lead levels increased from 3.3 µg/dL to 71.5 µg/dL without clinical signs of lead toxicity, and Burton's line was absent. The third cycle was discontinued due to elevated blood lead levels, and *Naga Bhasma* was withheld. Ayurvedic antidote therapy with *Ghrutkumari* (Aloe vera) and *Haridra* (Curcuma longa) was initiated, resulting in a marked reduction in blood lead levels from 71.5 µg/dL to 6.3 µg/dL. This case highlights the potential adjunctive role of this formulation in advanced malignancy while emphasizing the necessity of strict lead and renal monitoring and the use of GMP-certified preparations for safe clinical application.

Declarations

Ethical Approval: Informed consent was obtained from the patient for publication of this case report and

accompanying data.

Competing Interests: The authors declare no competing interests.

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