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Original Research Article

Classical ayurveda management of TCH (taxane, carboplatin, and herceptin) based chemotherapy induced peripheral neuropathy- A case report

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ABSTRACT

Although empirical data on the influence of Ayurveda on Chemo/Radiotherapy-induced side effects are limited, its methodological framework, grounded in a 'systems thinking' perspective, enables the precise delineation of the pathogenic stage of these side effects. This, in turn, facilitates the development of a strategy to address the decline in the quality of life parameters commonly associated with cancer treatment. Ayurveda personalized approach to disease management typically involves providing customized diets, lifestyle adjustments, medications, and detoxification therapies that target the entire body.

We present a case involving a patient with numbness and pain in the right hand after undergoing chemotherapy who was referred to us by an oncologist for symptom management. This case report demonstrates the Ayurveda approach for establishing the etiology, pathogenesis, pathophysiology, and treatment of Chemotherapy-Induced Peripheral Neuropathy (CIPN) resulting from taxane-based chemotherapy. Following Ayurveda intervention, the patient exhibited significant improvements in symptoms and quality of life parameters.

This case report systematically illustrates the application of Ayurveda approach in CIPN management.

1. Introduction

Chemotherapy-Induced Peripheral Neuropathy (CIPN) is a prevalent and dose-limiting side effect that affects a significant proportion of patients receiving treatment with six major antineoplastic agents, including platinum-based medications, taxanes, vinca alkaloids, epothilone proteasome inhibitors, and immunomodulatory drugs. Taxane is responsible for approximately 87% of toxicity associated with CIPN [1].

Taxane, Carboplatin, and Herceptin (Trastuzumab) are antineoplastic agents with a higher survival rate. However, they are associated with side effects such as peripheral neuropathy, myelosuppression, arthralgia, myalgia, and skin reactions that can adversely affect quality of life (QOL). These symptoms may be transient and subside after chemotherapy is completed or can be severe, resulting in dose reduction or cessation of therapy [2].

CIPN is a multifactorial manifestation with alterations in ion channel function and oxidative stress and has been linked to axonal degeneration, poor calcium homeostasis, neuroinflammation, and immune system activation [3]. Several risk factors have been identified for Taxane-induced CIPN, including pre-existing neuropathy, age >60 years, female sex, comorbidities such as diabetes mellitus, cumulative dose, infusion time, dose per cycle, and chemotherapy protocol [4,5].

Managing painful CIPN remains a significant challenge, and various pharmaceutical agents have been explored for treatment, including antidepressants, anticonvulsants, and the serotonin-norepinephrine reuptake inhibitor duloxetine. Conventional methods of CIPN management are associated with several adverse effects, such as nausea, dizziness, insomnia, and anxiety [6].

Ayurveda can offer effective management of taxane-based CIPN. In Ayurveda, naming the disease is not always possible. In such cases, the causative factors (*Samutthana vishesha*), site (*Adhisthana*), and nature of the disease (*Vikara prakruti*) are considered. Based on our experience,

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CIPN may be related to the *Raktavrita Vata/Supti* category of *Vatavyadhi*, which can be treated using principles derived from *Vatashonita*. The treatment principles for *Raktavrita* vata are similar to those for *Vatashonita*, making it a suitable candidate for treatment. (Cha.Chi 28/194).

In this report, we present a case of CIPN that was successfully managed with Ayurveda diet, lifestyle, medicines, and therapy.

2. Patient information

A 50-year-old South Indian woman presented with numbness in the right hand, occasional cramp-like pain at the surgery site, headache, photophobia, general tiredness, and vague body pain for 2 years. She presented with a history of carcinoma of the right breast in 2020, for which she underwent a right breast lumpectomy in July 2020 and was administered CT-RT (6 cycles of TCH Regimen (Docetaxel + Carboplatin + Trastuzumab) + 17 doses of Trastuzumab), completed in Aug 2021. She received Oral Tamoxifen (20 mg), an estrogen receptor modulator, following chemotherapy. The patient was doing well symptomatically; she gradually developed symptoms of pronounced neuropathy with the symptoms as mentioned above–2-3 months post-surgery, followed by chemotherapy.

Her medical history revealed frequent episodes of throbbing pain in the head associated with heaviness, irritation to sound, and light for 30 years, which was diagnosed as migraine. The patient had no history of diabetes mellitus or hypertension. To address the symptoms of CIPN and improve quality-of-life parameters, medical oncologists referred her to Sri Shankara AyurVAID Center for Integrative Oncology Department.

3. Clinical findings

Clinical examination revealed normal cardiovascular and respiratory system findings. Sensory examination revealed the absence of superficial touch, and the presence of hot and cold discrimination, pinprick, and vibration. Additionally, deep tendon reflexes decreased in the right biceps, triceps, and supinator muscles. The numbness in the right upper limb was moderate, while it was low in the left upper limb. The patient's weight was 68.5 kg with a BMI of 27.7 kg/m.

4. Timeline

It is followed as given in Table 1.

5. Diagnosis and Diagnostic assessment

Classical Ayurveda diagnosis was based on clinical examination involving *Trividha*, *Ashtavidha*, *Dashavidha*, and detailed *Srotas pariksha*, leading to precise *Samprapti*. The neurotoxic effects of TCH-based chemotherapeutic agents are due to their *Ushna, Teekshna, Vyavayi guna*, and other nidana-like intake of foods such as *Ruksha, Laghu* (jowar, oats without oil), *Ushna, Katu* (Horsegram sprouts, red chillies, onion, garlic), and amla rasa pradhana (Tamarind, Citrus fruits). These factors aggravate Vata (manifesting as axonal damage of dorsal root ganglion) and *Pitta Rakta dusti* (manifesting as increased oxidative stress and inflammatory responses) leading to *Rasa dhatu dusti* (manifesting as mitochondrial damage) and uttarottara dhatu dusti such as *Rakta*, *Mamsa*, *Meda*, *Asthi, Majja* and upadhatus such as *Sira* and *Snayu* (microtubule disruption and intraepidermal nerve fiber loss terminal arbor degeneration) leading to *Raktavrita Vata*.

The assessment was performed at predefined intervals spanning over 5 months. The evaluation criteria included the standard outcome parameters such as the CTCAE scale, EORTC – QLQ- CIPN20, mTNS score, and FACT Taxane scoring.

Table 1
Timeline followed.

2022-04-24	First Visit- Initial consultation and screening, existing risk explained and plan of management advised
2022-08-24	2nd Visit, Panchakarma treatment was advised. Treatment objective discussed
2022-09-21	External therapies and internal medications are prescribed.
2022-10-05	Treatment completed. Gradual relief in symptoms such as paresthesia, Headache, Backpain, Fatigue, and Arthralgia
2023-01-24	A follow-up consultation was done, The Patient is doing better. Internal medications revised
2023-03-21	Review consultation is done. Medications are advised to maintain general health.
2024-01-11	Review done on call (telephonic). The patient is doing well. Symptoms are relieved.

6. Therapeutic interventions

The patient was diagnosed with *Raktavrita Vata*, and treatment was planned, which included a combination of internal medications as well as a combination of external therapies and systemic cleansing.

The treatment was repurposed from *Vatashonita chikitsa siddhanta*, which consisted of Dhara with *Dashamoola Ksheera, Virechana* with Avipatti Churna, and Matra Basti with Dhanvantarm mezhupakam. *Shirodhara*, with *Ksheerabala Tailam*, and *Nasyam* with *Anutaila*.

Internal medication Pathyakshadhatrayadi Kashayam, Dhanvantaram Gulika, Yogaraja Guggulu, and Brihat Triphala Churnam were administered during the treatment. At discharge, *Brahma Rasayana* was advised as Rasayana medication for 60 days (Supplementary Table 1).

7. Follow-up and Outcomes

Clinical symptoms gradually resolved by the end of 15 days of intervention. The standard outcome scale CTCAE showed improvement in paresthesia (Grade 2 to grade 1), headache (Grade 2 to Absent), back pain (Grade 1 to Absent), fatigue (Grade 2 to Absent), arthralgia (Grade 2 to Grade 1) and numbness from grade 2 to 1 at the end of the 18th day. EORTC – QLQ- CIPN20 reduced from 30/76 to 18/76. FACT-Taxane Scoring improved from 117.5 to 147.6 indicating the improved QOL (Supplementary Tables 2, 3, 4, 5,6). Follow-up was done on 11.01.2024 where the patient conveyed that through out the year, she was in state of well being. Her appetite improved, sleep patterns were regular, and bowel movements were consistent. She reported being content with energy levels and had not experienced any symptoms of CIPN.

Another follow-up was done on 15.07.2024 via telephone conversation. The patient had lost 3–4 kg of weight and was currently weighing 63 kg.

8. Discussion

Taxane-induced neurotoxicity is known to impair somatosensory nerves and result in the development of neuropathic pain, which can be attributed to microtubule disruption and axonal transport impairment. This knowledge can be applied to the Ayurveda concept of *Pitta* and *Vata doshasanchaya*, which refers to the cumulative toxicity caused by chemotherapy and its impact on body tissues and systems. This toxicity can lead to a condition known as *Rasadusti*, which affects the consecutive *Dhatus* (tissues) of *Rakta, Mamsa, Meda, Asthi, Majja*, and the *Upadhatus* (accessory tissues) such as *Sira* (Blood vessels), *Kandara* (Tendons), *Snayu* (Ligaments and Nerves), and *Twak* (Skin). This is because of the *teekshna, ushna, vyavayi*, and *vikasi* guna of taxane-based agents. As a result of this cumulative toxicity, a cellular scenario can develop that resembles *Raktavrita Vata* [7]. Therefore, *Chikitsa* (treatment) should primarily address each component of samprapti (etiopathogenesis) and aim to clear the interlacing pathways leading to *Avarana* (blockage).

The symptoms of *Raktavrita Vata*, are characterized by *Daha* (burning sensation in the extremities), *Harsha* (numbness), *Arati* (intense pain resembling a shock), *Pipeelikanam Cha Sanchara* (ant

crawl-like sensation), and various forms of pain, as well as muscle weakness, are akin to those of CIPN. The primary goal in this case was to eliminate the obstacles posed by *Pitta* and *Rakta* dosha first, followed by maintaining control over the aggravation of *Vata* [8].

Effective management of CIPN may involve strategies such as reducing or delaying the use of microtubule targeting agents/taxanes or, in severe cases, discontinuing treatment altogether, which could impact the overall prognosis. However, CIPN can be managed effectively through the application of Ayurveda principles.

In this case, there was a significant improvement in the patient's clinical complaints of CIPN. Extended follow-up observations showed that these improvements were sustained.

Dashamoola ksheeradhra as *Purva karma* was planned to improve microcirculation. As seka is a *Snigdha* sweda (moist sudation), it pacifies *Vata* by *Sneha* and *Ushna guna* [9] and may pacify inflammation and minimize irritation and nerve tissue compression.

The *Virechana karma* greatly helped in *Pittashodhana* (eliminating Pitta dosha from the body).

Virechana is a therapeutic purgation that aids in eliminating excess *Pitta* and stimulates nerve endings, thereby increasing the activity of the myenteric plexus and reducing systemic inflammation in the gut [10].

Basti is commonly used to address the vitiation of *Vata* dosha. However, it is important to note that Basti is not limited to the GIT and can have systemic benefits, as indicated by *Phalashruti* of *Basti*. This is significant in light of the well-established Gut-Brain Axis (GBA) theory, which posits that neuroimmune-endocrine mediators play a role in communication between GBA. Additionally, gut bacteria can influence the gut-brain axis [11].

Nasya, a therapeutic intervention, has been used to alleviate symptoms of neuropathy. The administration of drugs through the nasal route stimulates the olfactory nerve and higher brain centers, resulting in regulation of the endocrine and nervous systems [12]. *Shirodhara*, a therapeutic procedure, was planned to mitigate aggravated *Vata* and alleviate stress [13]. *Shirodhara* is effective in reducing anxiety and other psychological conditions, sleeplessness, and improving sleep duration and quality, as per research studies [14].

The Internal medication Pathyakshadhatrayadi Kashayam possesses anti-inflammatory properties and has been traditionally used to pacify *Pitta* and *Vata* [15]. Similarly, Dhanvantaram Gutika has been found to exhibit anti-inflammatory activity [16] These findings highlight the potential of Ayurveda as a complementary and integrative model to address the side effects of conventional cancer treatments, such as chemotherapy, in both the acute and delayed phases.

Although this case report provides limited data, it is important to note that it is not possible to draw broad conclusions based on a single case study, and the focus on the subjective response to treatment further narrows the scope of potential findings. The case study is related to an important area despite the lack of an objective assessment. NCS, but the case has been documented using standard outcome scales and patient-reported outcomes.

This case report highlights the application of *Ayurveda* in managing taxane-induced peripheral neuropathy in a patient undergoing TCH chemotherapy, with impressive outcomes.

The use of a single-system approach to manage the side effects of taxane-based chemotherapy is limited. Therefore, an integrative approach led by *Ayurveda* could provide a potential solution. This finding underscores the need for further research in integrative oncology to identify more effective care models.

9. Patient perspective

05.10.2022: The patient was satisfied with the treatment and care provided at the hospital. She is now able to perform routine activities without discomfort.

24.08.2023: In-person visited her Medical Oncologist for Physical routine check-up and Ayurveda department for follow-up; No fresh complaints, she has been active, with good energy levels.

11.01.2024: The patient conveyed during the face-to-face encounter that the previous year had been favorable. Her appetite improved, sleep patterns were regular, and bowel movements were consistent. She reported being content with energy levels and had not experienced any symptoms of CIPN. Moreover, she expressed feeling more relaxed and optimistic.

15.07.2024: Telephonic: I have made notable progress in my weight loss journey, shedding 3–4 kg and currently weighing 63 kg. I am maintaining a healthy diet and lifestyle as directed by my doctor.

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Declaration of generative AI in scientific writing

The authors declare that they have not used artificial intelligence (AI) tools for writing and editing the manuscript, and no images were manipulated using AI.

Author contributions

Primary consultant and Conceptual ideation by Dr. Zankhana Buch; Data collection and documentation was done by Dr. Aishwarya Lakshmi, Dr. Swathi Bhat; Writing, Editing, and Reviewing of manuscript done by Dr. Suprabha Hegde and Dr. Zankhana Buch.

Informed consent

The informed consent regarding documentation and publication of the case was obtained from the patient.

Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaim.2024.101044.

References

[1] Eckhoff L, Knoop A, Jensen MB, Ewertz M. Persistence of docetaxel-induced neuropathy and impact on quality of life among breast cancer survivors. Eur J Cancer 2015;51(3):292–300. https://doi.org/10.1016/j.ejca.2014.11.024.

[2] Forsyth PA, Balmaceda C, Peterson K, et al. Prospective study of paclitaxel-induced peripheral neuropathy with quantitative sensory testing. J Neuro Oncol 1997;35:47–53. https://doi.org/10.1023/a:1005805907311.

[3] Salat K, Moniczewski A, Librowski T. Nitrogen, oxygen or sulfur containing heterocyclic compounds as analgesic drugs used as modulators of the nitroxidative stress. Mini-Rev Med Chem 2013;13:335–52. https://doi.org/10.2174/1389557511313030003.

[4] Argyriou AA, Kyritsis AP, Makatsoris T, Kalofonos HP. [5] Chemotherapy-induced peripheral neuropathy in adults: a Comprehensive update of the literature. Cancer Manag Res 2014;6:135–47. https://doi.org/10.2147/CMAR.S44261.

[5] Iltenburg NC, Boogerd W. Chemotherapy-induced neu-[6] ropathy: a comprehensive survey. Cancer Treat Rev 2014;40:872–82. https://doi.org/10.1016/j.ctrv.2014.04.004.

[6] Park K, Kim S, Ko YJ, Park BJ. Duloxetine and cardiovascular adverse events: a systematic review and meta-analysis. J Psychiatr Res 2020;124:109–14. https://doi.org/10.1016/j.jpsychires.2020.02.022.

[7] Shukla V., editor Vaidyamanorma Hindi Commentary on Charaka Samhita of Charaka, Chikitsasthana; Chapter 28. Verse, 63. editors, (1 st ed). Varanasi: Chaukhamba Prakashan. p. 619–620.
[8] Gupta KA, editor. Commentary Vidyotini on Ashtanga Hridaya of Vagbhata, Nidanasthana: Chapter 16 Verse 33. edition 2019. Varanasi: Chaukhamba Prakashan; 2009. p. 538.
[9] Paradkar Bhisagacharya Harisastri, editor. Commentaries Sarvanga Sundara of Arundatta and Ayurveda Rasayani of Hemadri on Astanga Hridaya of Vagbhata, Sutrasthana; Chapter 12 Verse 14. Varanasi: Chaukhambha Orientalia; 2005. p. 153.
[10] Chaturvedi A, Rao PN, Kumar MA, Ravishankar B, Rao N, Ravi M. Effect and mechanism of Virechana karma (Therapeutic purgation) over fructose-induced metabolic syndrome: an experimental study. Evid Based Complement Alternat Med 2016;21(3):194–201. https://doi.org/10.1177/2156587215596283.
[11] Gershon MD. Transplanting the enteric nervous system: a step closer to treatment for Aganglionosis. Gut 2007;56(4):459–61. https://doi.org/10.1136/gut.2006.107748.
[12] Radhika C, Kumar GV, Mihirjan K. A randomized controlled clinical trial to assess the efficacy of Nasya in reducing the signs and symptoms of cervical spondylosis. Ayu 2012;33(1):73–7. https://doi.org/10.4103/0974-8520.100316.
[13] Gupta Kaviraj Atridev, editor. Commentary Vidyotini on Ashtanga Hridaya of Vagbhata, Sutrasthana: Chapter 22 Verse 24. edition 2019. Varanasi: Chaukhamba Prakashan; 2009. p. 182.
[14] Pokharel S, Sharma AK. Evaluation of insomrid tablet and Shirodhara in the management of anidra (Insomnia). AYU 2010;31:40–7. https://doi.org/10.4103/0974-8520.68209.
[15] Vidyasagar Pandit P, editor. Samhita of Sharangdhara, Madhyama khanda; Chapter 2 Verses 143-145. Varanasi: Chaukhamba Surbharati Prakashan; 2013. p. 220.
[16] Krishnan vaidyan KV, Gopala Pillai S, editors. Commentory Sujanapriya Vyakhya on Sahasrayogam, Mullakal. 29 th ed. Vidyarambham. Publishers; 2006. p. 236.