Case Report
COVID-19 patient with B cell lymphoma co-morbidity managed with co-administration of ayurvedic formulation

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1. Introduction
There is no gold standard therapeutic agent proven for COVID-19 and world is still facing health emergency of COVID-19 pandemic/endemic. Cohort studies have reported higher mortality rates in COVID-19 patients with cancer [1,2]. Increased mortality is observed in COVID-19 patients with lymphoma because of immune-compromised status due to the disease and/or its treatment with immune-chemotherapy [3]. Here we report a mild COVID-19 case with lymphoma treated in home quarantine with integrated treatment. Ayurvedic understanding of COVID-19 is reported as 'exogenous fever' later resulting in systemic involvement with vata-kapha dosha profile and pitta dosha as adjuvant [4]. Case reports and trials of Ayurveda interventions in mild to severe COVID-19 cases are published [5,6]. This is perhaps the first reported case of COVID-19 with cancer (B Cell lymphoma) treated with integrated approach and Ayurveda medicine and resulted RT-PCR negative in a week.

2. Patient information
2.1. De-identified patient specific information
A 47 year old shopkeeper patient from Mumbai started fever and Malaise on 12th June 2020. It was early first wave of COVID-19 pandemic in Mumbai. He was asked for RT-PCR examination of nasal swab and was found to be negative. Plethora of literature is available on anti-viral and immunomodulatory efficacies of Ayurveda herbs based on in vitro studies. Such efficacies can be replicated at patient’s level if supported with wisdom of Ayurveda epistemology. Early diagnosis on RT-PCR and early inception of ayurveda medicine and diet interventions might be crucial element for better recovery.

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2.4. Relevant past interventions and their outcomes

Patient was diagnosed with B Cell lymphoma and was recently underwent 3 cycles of chemotherapy. Protocol included R–CHOP regimen containing rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone.

2.5. Clinical findings

Relevant clinical examination and other findings: Patient started fever (104 ° F) on 12th June 2020. There was also severe malaise, catarrh and anosmia. His consultation was done on a video call and was recommended to stay in home quarantine. The treatment was started early and thus patient did not landed in stage of lower respiratory complications. Oxygen levels were asked to be examined meticulously and to report in case of any deterioration and no fall in oxygen below 95% was observed during whole course. Patient was obese with height 168 cm, weight 96 kg with BMI of 34. It was a vatakaphasannitpata jwara with pittanubandhatva. There was decline in agni (metabolism), utsaha (enthusiasm) and bala (energy) evident clinically.

2.6. Diagnostic assessment

Diagnostic Testings: As patient had classical presentation of fever with anosmia, he was advised RT-PCR for COVID-19 and was found to be positive. Oxygen saturation was 96%. Hemoglobin level was 13.4 gm/dl and platelets were 2.15 million/cmm. CRP level was 13. Neutrophil/Lymphocyte ratio was not altered and leucocytes
value was 8000/cmm. Urine report were within normal limits. Patient responded well to management and oxygen saturation remained above 95% for whole course of disease.

**Diagnostic Challenges:** It was first wave of COVID-19 and national lockdown in India. Patient was in home isolation and thus thorough physical assessment was not possible.

**Differential Diagnosis:** Patient presented with fever with anosmia and ageusia. RT-PCR confirmed the diagnosis of COVID-19. Possibility of dengue was ruled out by normal Neutrophil count and normal platelet counts observed in hemogram. Ayurveda diagnosis was vata kapha pradhana jwara.

**Prognosis:** Patient was in immune-compromised state as he was on chemotherapy for his B cell Lymphoma. His ECOG score was 1. Early confirmation of COVID-19 on RT-PCR and early commencement of treatment helped in better prognosis of COVID-19. Oxygen levels remained maintained above 95% during the disease course. There were no any respiratory symptom like dyspnoea, sore throat, cough or any other symptoms associated with COVID-19 till eighteenth day. On third day temperature was at peak. This was perhaps indicative of ‘pachyamana jwara’ (ayurvedic concept referring a last surge in temperature before its decline) which was followed by sweating. On fifth day all the symptoms subsided except anosmia and ageusia and patient was found negative on RT-PCR on seventh day. Patient’s agni (metabolism), utsaha (enthusiasm) and bala (energy) returned to normal by tenth day.

**2.7. Changes in interventions with rationale**

The patient was recommended: 1) Madhav Rasayan (250 mg twice a day) for a week 2) Tab. Paracetamol 500 mg twice a day for first three days. After seventh day as RT-PCR was negative, it was continued for ten more days one tablet a day. Paracetamol in 500 mg dosage was used twice a day for first three days. Patient was also was asked to take vitamin C tablets in 500 mg dosage twice a day for first seven days and once a day for next 10days. Patient was recommended to take green gram soup by boiling roasted green grams in 14 parts of water till it obtains semisolid consistency for dinner. He was also asked to drink hot water for first three days. After seventh day patient was asked to resume his regular diet. Hot water steams and gargles were advocated for a week (Table 1).

**3. Follow-up and outcomes**

**3.1. Clinician and patient assessed outcome**

Body ache was relieved on second day with medication. Catarrh and malaise were not there after 3rd day of medication. Green gram soup and hot water helped in restoring agni (metabolic fire). On sixth day fever was completely relieved and taste and smell restored partially. On seventh day nasopharyngeal swab RT-PCR was found negative. Oxygen saturation remained maintained above 95% during whole course of disease. Details are mentioned in Table 2.

**3.2. Important follow up diagnostic tests**

Telephonic follow-up was taken every day. Outcomes were good as symptoms were relieved and no form of deterioration or complication was observed. Patient visited the clinic on 8th day and was found to be healthy on clinical examination.
3.3. Intervention adherence/tolerability

Intervention was well tolerated by patient. Ayurveda formulation was in tablet form and thus palatable. Patient was already on ayurveda medicines and hence was compatible with the prescribed medications and pathya (dietary dos and don'ts) food regimes.

3.4. Adverse effects

No adverse effects were not observed.

4. Discussion and remarks

4.1. Strengths and limitations of case

Patient was in home quarantine and thus daily charts of vitals and biochemistry reports are not available. Among inflammatory markers only CRP was evaluated. As patient was responding well, we did not evaluate more inflammatory markers like Interlukin-6. Thorough physical examination was not possible as patient was in home isolation. Apart from these limitations, this is perhaps the first reported case of COVID-19 with active cancer and treated with integrated approach. Immunosuppression (whether caused by the disease itself or the treatment) can lead cancer patients to serious complications requiring hospitalizations and affected disease prognosis [7]. Patients with cancer are more susceptible to COVID-19 and also show increased mortality as reported in systematic review [8]. Another meta-analysis reports higher risk of severe disease and death outcomes from COVID-19 infection as compared with general COVID-19 populations [9]. Thus treating a patient with such prominent co-morbidity like cancer is a strength of this case report.

In this case integrated management helped in better outcomes and did not necessitate hospitalization. Patient was in Home isolation and we repeated RTPCR on 7th day (instead of a repeating it after 14 days as per trend in first Covid-19 wave). Interestingly we found it negative implying anti viral effects of treatment and also early clearance of viral particles. RT-PCR was found to be negative on seventh day implying anti-viral effects of treatment and also early clearance of viral particles. In this case initial CRP value was 13. According to another systematic reviews and meta-analysis raised CRP is associated with poor prognosis in COVID and also early clearance of viral particles. RT-PCR was found to be positive after 14 days as per trend in report. In this case initial CRP value was 13. Another meta-analysis reports higher risk of severe disease and death outcomes from COVID-19 infection as compared with general COVID-19 populations [9]. Thus treating a patient with such prominent co-morbidity like cancer is a strength of this case report.

This was a COVID-19 case with active B cell lymphoma. Now there is enough evidence that Gut-Brain axis is not mere bidirectional but a cluster including immune, endocrine and metabolic components [37]. Concept of Agni is pivotal in Ayurveda pathophysiology and deepana (medicines enhancing 'agni' including appetizers) and pachana (medicine improving metabolism) are pivotal in practise of Ayurveda medicine.

Ayurvedic understanding of cytokine storm can be inflammation involving vitals is Dhatu-paka (histological and functional deregulation of body tissue) according to ayurveda. Anti-inflammatory, immuno-modulatory evidences of Ayurveda herbs and their actions on particular cytokines are well documented [16]. Ayurveda Classical literature obviously do not mention Cytokine storm. However the phenomenon of inflammation is referred as Dhatu-paka (histological and functional derangement of body tissue) in Ayurveda. Many ayurveda herbs are proven anti-inflammatory, immunomodulatory and also having effects on cytokines [17]. Madhav Rasayan is a formulation with most of ingredients having rasayana, Anti-inflammatory and immuno-modulatory efficacies.

5. Scientific rationale for conclusions

Use of immunomodulators achieving Th1/Th2 equilibrium and immune homeostasis for COVID-19 is reported in literature [18,19]. Madhav Rasayan is such formulation aimed at immune homeostasis. Along with immunomodulatory, it is mixture of herbs with anti-viral, anti lung fibrotic, anti coagulative activities. There are evidence of designer drugs involving safer, curative and synergistic combinations as multiple immune-modulating strategies are necessary to achieve clinical success owing to complex interplay between pathways [20]. Madhav Rasayana is a formulation with such synergy with ingredients as Piper longum, Glycyrhriza glabra, Eclipta alba, Achyranthes aspera, Embelia ribes and Aloe vera. Glycer- erine in Glycyrriza glabra is reported to neutralize SARS CoV 2 [21]. Phytochemicals from all ingredients have shown immunomodulatory efficacies in silico/in vitro models [22–29]. Phytochemicals from Glycyrriza glabra, E. alba, P. longum and A. vera are having efficacies for lung damage/fibrosis [30–33]. Embelin in embilia ribes is a PKC inhibitor and possesses antiplatelet and antithrombotic effects [34].

In Ayurvedic viewpoint, P. longum and Glycyrriza glabra is the combination to be used in infective respiratory conditions. E. alba is the key herb aimed at minimizing complications of COVID-19 which are result of inflammatory and coagulative pathologies. E. alba helps in maintaining 'Rakta-Pitta-Prana' homeostasis and for reducing Dhatu-paka i.e. inflammatory pathologies which are attributed to pitta dosha [35]. E. alba helps in maintaining Raktu (body tissue resembling and inclusive of Blood) - Pitta (Dosha required for digestion and tissue and molecular level metabolism) - Prana (vitality element and oxygen) homeostasis as it reduces Dhatu paka (inflammation in vital tissues) by alivating pitta which is reported to cause all inflammatory pathologies.

5.1. Patient perspective

On 12th June I started feeling running nose, fever and was unable to sense smell and taste. It was pandemic first wave in Mumbai and I suspected as loss of smell was COVID symptom. I consulted my Ayurveda doctor. I also had telephonic opinion from my allopathic physician. I opted to get tested for COVID-19 and was found positive. I was frightened as there was chaos and strict lockdown in the city. There was a good amount of fear factor, but at the same time I had belief in my Ayurveda doctor as I was his patient for CKD and Lymphoma in earlier times. I had personal experiences that ayurvedic treatment is effective. The doctor recommended to
take Vitamin C, Paracetamol and Ayurveda preparation Madhav Rasayan tablet. He confirmed if I had sore throat or cough or dyspnea which was not there. I was also recommended hot water steams and gurgles and a specific ayurveda diet. I was keeping records of my oxygen levels which never dropped below 95% fortunately. After 3rd day of taking the medicine I started feeling almost well. On 7th day I repeated RTPCR test and it turned out to be negative. Thankfully no complications like cough or breathing issues happened and I got my illness resolved in almost a week. Thanks to Ayurveda treatment and my doctors.

5.2. Take away lesson

Immune dysregulation is key component in both inflammatory pathologies like COVID-19 and cancer for which ayurveda interventions are reported to be effective [35,36]. This was a COVID-19 case with B cell lymphoma. Early diagnosis on RT-PCR and early inception of ayurveda interventions and ayurveda diet recommendatons might be crucial element for better recovery. Immunomodulatory efficacies of many herbs are reported using many in vitro models, but if supported with ayurvedic understanding of disease and Ayurveda principles of internal medicine, the results can replicated on patients level. This is perhaps first reported case of COVID-19 with cancer managed with Ayurveda and thus underlines importance of integrated approach for preventing COVID-19 patients from bad prognosis.

Informed consent

Informed written consent was obtained from the patient for publication.

Author contributions

Dr. Prasad Pandkar and Dr. Santosh Deshmukh were physicians treating patient and wrote the manuscript. Dr. Vinay Sachdev was assistant physician and also contributed in writing the manuscript.

Conflict of interest

None.

References

[1] Anil I, Arnold R, Benkwitz-Beford S, Bransford S, Campton N, Cazier J-B, et al. The UK Coronavirus Cancer Monitoring Project: protecting patients with cancer in the era of COVID-19. Lancet Oncol 2020;21:622–4. https://doi.org/10.1016/S1470-2243(20)30230-8.
[2] Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Rivera DR, et al. Clinical impact of COVID-19 on patients with cancer (CC19): a cohort study. Lancet 2020;395:1907–18. https://doi.org/10.1016/S0140-6736(20)31187-9.
[3] Lamure S, Dulery R, Di Blasi R, Chauvet A, Laureana C, Deau-Fischer B, et al. Determinants of outcome in COVID-19 hospitalized patients with lymphoma: a retrospective multicentric cohort study. EClincMedicine 2020;27:100545. https://doi.org/10.1016/j.eclim.2020.100549.
[4] Pathiyadath R, Kataria S, Payyappallimana U, Mangalath P, Namportyin V, Sharma P, et al. Ayurvedic clinical profile of COVID-19 – a preliminary report. J Ayurveda Integr Med 2020. https://doi.org/10.1016/j.jaim.2020.05.011.
[5] Jamadagni DS, Pandkar DP, Saundankar DT, Shirsage DC, Malekar S. Efficacy of Madhav rasayan plus as adjuvant in moderate COVID-19 patients: preliminary outcomes of randomized controlled trial. J Ayurveda Integr Med 2022;100050. https://doi.org/10.1016/j.jaim.2022.100050.
[6] Rastogi S. Ayurveda co-interventions have supported complete recovery in severe covid-19 infection with a chest severity score 18/25: a case report. J Ayurveda Integr Med 2021. https://doi.org/10.1016/j.jaim.2021.02.008.
[7] Al-Quetmeat OM, Amer AM. The impact of the COVID-19 pandemic on cancer patients. Am J Clin Oncol 2020;43:452–5. https://doi.org/10.1097/COC.0000000000000712.
[8] Yang L, Chai P, Yu J, Fan X. Effects of cancer on patients with COVID-19: a systematic review and meta-analysis of 63,019 participants. Cancer Biomark 2021;18:298–307. https://doi.org/10.3233/CBM-200395.2020.0559.
[9] Han Q, Zhang Q, Chou J, Tan SH, Chua COV Y, Cai J. Impact of COVID-19 on the outcomes of diagnoses with patients with COVID-19: a systematic review and meta-analysis. BMJ Open 2022;12:e044661. https://doi.org/10.1136/bmjopen-2020-044661.
[10] Fachmany GM, Hashemi S, Styczynski J, Khafarran-Dabaja MA, Alblooshi BM, de la Cámara R, et al. The risk and prognosis of COVID-19 infection in cancer patients: a systematic review and meta-analysis. Hematol Oncol Stem Cell Ther 2020. https://doi.org/10.1016/j.hemonc.2020.07.006.
[11] Ending isolation and precautions for people with COVID-19: interim guidance. https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html. [Accessed 12 July 2022].
[12] No Title n.d. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf?#_a23C;Text: Using available preliminary data%2C severe or critical disease. (accessed July 12, 2022).
[13] Tahagholi-Hajighorbani S, Zafari P, Masouemi E, Rajabinejad M, Jafari-Shabik R, Hasanl B, et al. The role of dysregulated immune responses in COVID-19 pathogenesis. Virus Res 2020;290:198197. https://doi.org/10.1016/j.viruses.2020.198197.
[14] Pandkar PD, Sachdeva V. Pathophysiology of COVID-19 and host centric approaches in Ayurveda. J Ayurveda Integr Med 2022;13:100380. https://doi.org/10.1016/j.jaim.2022.11.010.
[15] Jantan I, Ahmad W, Bukhari SNA. Plant-derived immunomodulators: an insight on their preclinical evaluation and clinical trials. Front Plant Sci 2015;6:305. https://doi.org/10.3389/fpls.2015.00305.
[16] Trikamji J, editor. Charak samhita of agnivesha Part 2. 1 st. Varanasi: ChaukambaSurbharati Prakashana; [n.d].
[17] Tillu G, Chaturvedi S, Chopra A, Patwardhan B. Public health approach of ayurveda and yoga for COVID-19 prophylaxis. J Alternative Compl Med 2020;26:360–4. https://doi.org/10.1016/j.jaim.2020.01.025.
[18] Tillu G, Salvi S, Patwardhan B. AYUSH for COVID-19 management. J Ayurveda Integr Med 2020;11:95–6. https://doi.org/10.1016/j.jaim.2020.06.012.
[19] Patwardhan B, Gautam M. Botanical immunomodulators: scope and opportunities. Drug Discov Today 2005;10:495–502. https://doi.org/10.1016/S1359-6464(04)03357-4.
[20] van de Sand L, Bormann M, Alt M, Schipper L, Heilingloh CS, Steinmann E, et al. Glycyrrhizin effectively inhibits SARS-CoV-2 replication by inhibiting the viral main protease. Viruses 2021;13:609. https://doi.org/10.3390/v13040609.
[21] Bordhar N, Karimi MH, Amighrokhf Z. The effect of glycyrrhizin on maturaion and T cell stimulating activity of dendritic cells. Cell Immunol 2012;280:44–9. https://doi.org/10.1016/j.cellimm.2012.11.013.
[22] Lee JY, Lee J-H, Park JH, Kim S-Y, Choi JY, Lee SH, et al. Liqueuritigenin, a licorice flavonoid, helps mice resist disseminated candidiasis due to Candida albicans by TH1 immune response, whereas liqueurit, its glycoside form, does not. Int Immunopharm 2009;9:632–8. https://doi.org/10.1016/j.intimp.2009.02.007.
[23] Lee H-S, Kim E-N, Jeong G-S. Oral administration of licoritigenin confers protection from atopic dermatitis through the inhibition of T cell activation. Biomolecules 2020;10:876. https://doi.org/10.3390/biom10050876.

9. https://doi.org/10.1016/j.cellimm.2012.11.013.
[24] Lee JY, Lee J-H, Park JH, Kim S-Y, Choi JY, Lee SH, et al. Liqueuritigenin, a licorice flavonoid, helps mice resist disseminated candidiasis due to Candida albicans by TH1 immune response, whereas liqueurit, its glycoside form, does not. Int Immunopharm 2009;9:632–8. https://doi.org/10.1016/j.intimp.2009.02.007.

9. https://doi.org/10.1016/j.cellimm.2012.11.013.
[25] Lee JY, Lee J-H, Park JH, Kim S-Y, Choi JY, Lee SH, et al. Liqueuritigenin, a licorice flavonoid, helps mice resist disseminated candidiasis due to Candida albicans by TH1 immune response, whereas liqueurit, its glycoside form, does not. Int Immunopharm 2009;9:632–8. https://doi.org/10.1016/j.intimp.2009.02.007.

9. https://doi.org/10.1016/j.cellimm.2012.11.013.
[26] Lee JY, Lee J-H, Park JH, Kim S-Y, Choi JY, Lee SH, et al. Liqueuritigenin, a licorice flavonoid, helps mice resist disseminated candidiasis due to Candida albicans by TH1 immune response, whereas liqueurit, its glycoside form, does not. Int Immunopharm 2009;9:632–8. https://doi.org/10.1016/j.intimp.2009.02.007.
[33] Sun Z, Yu C, Wang W, Yu G, Zhang T, Zhang L, et al. Aloe polysaccharides inhibit influenza A virus infection—a promising natural anti-flu drug. Front Microbiol 2018;9. https://doi.org/10.3389/fmicb.2018.02338.

[34] Li JY, Chen RJ, Huang LT, Lee TY, Lu WJ, Lin KH. Embelin as a novel inhibitor of PKC in the prevention of platelet activation and thrombus formation. J Clin Med 2019;8:1724. https://doi.org/10.3390/jcm8101724.

[35] Sumantran VN, Tillu G. Cancer, inflammation, and insights from ayurveda. Evidence-Based Complement Altern Med 2012;2012:1–11. https://doi.org/10.1155/2012/306346.

[36] Anderson R, Rapoport BL. Immune dysregulation in cancer patients undergoing immune checkpoint inhibitor treatment and potential predictive strategies for future clinical practice. Front Oncol 2018;8. https://doi.org/10.3389/fonc.2018.00080.

[37] Boulangé CI, Neves AL, Chilloux J, Nicholson JK, Dumas ME. Impact of the gut microbiota on inflammation, obesity, and metabolic disease. Genome Med 2016;8:42. https://doi.org/10.1186/s13073-016-0303-2.