

Photobiomodulation in Stevens-Johnson Syndrome in a Metastatic Breast Cancer: Case Report

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Fotobiomodulação na Síndrome de Stevens-Johnson no Câncer de Mama Metastático: Relato de Caso

La Fotobiomodulación en el Síndrome de Stevens-Johnson en el Cáncer de Mama Metastático: Informe de Caso

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ABSTRACT

Introduction: Stevens-Johnson syndrome is a rare but potentially fatal condition, which requires early diagnosis and treatment to ensure good prognosis. Due to the complexity of the syndrome and the lack of a standard wound care treatment, the use of photobiomodulation has been discussed. **Case report:** A 30-year-old woman with metastatic breast cancer and Stevens-Johnson and Li-Fraumeni Like syndromes using photobiomodulation as an adjuvant strategy in the treatment of pain and skin wounds. The erythematous cutaneous lesions involved almost the entire body surface with painful, scaly, crusted and bullous lesions with bleeding spots in the posterior region of both ears lobes and in the occipital region which made it difficult to accommodate the patient in lateral decubitus and in semi-recumbent position. Two photobiomodulation applications (red, with a wavelength of 660 nm) were performed, where lesions in the occipital region and ears were treated with a dose of 2 Joules per point and 4 Joules in the scapular region for pain relief (infrared, with a wavelength of 808 nm), followed by mobilization and myofascial release in the scapular region. In 48 hours, the cutaneous lesions reduced, and the pain improved, which facilitated the adequate and painless positioning in bed. After 15 physiotherapy sessions, the patient was discharged. **Conclusion:** Photobiomodulation has been shown to be effective in the complementary treatment of the acute phase of Stevens-Johnson Syndrome regarding tissue regeneration and analgesia.

Key words: Stevens-Johnson syndrome; low-level light therapy; breast neoplasms; physical therapy specialty.

RESUMO

Introdução: A síndrome de Stevens-Johnson é uma condição rara e potencialmente fatal que requer diagnóstico precoce e tratamento adequado para garantir bom prognóstico. Em virtude da complexidade da síndrome e da falta de tratamento padrão para as feridas, o uso da fotobiomodulação tem sido discutido. **Relato do caso:** Mulher, 30 anos, com câncer de mama metastático, portadora das síndromes de Stevens-Johnson e de Li-Fraumeni Like, em uso da fotobiomodulação como estratégia adjuvante no tratamento da dor e das feridas na pele. As feridas cutâneas eritematosas envolveram quase toda a superfície corpórea, com lesões escamosas, crostosas e bolhosas, dolorosas, com pontos hemorrágicos em região posterior de ambos os lóbulos das orelhas e na região occipital, dificultando a acomodação da paciente em decúbito lateral e em posição semirreclinada. Foram realizadas duas aplicações da fotobiomodulação (vermelho, com comprimento de onda de 660 nm) nas regiões occipital e de orelhas, com dose de 2 Joules por ponto; e 4 Joules em região escapular para analgesia (infravermelho, com comprimento de onda de 808 nm). Ambas as aplicações foram seguidas de mobilização e liberação miofascial na região escapular. Em 48 horas, houve regressão das lesões cutâneas e melhora da dor, facilitando posicionamento adequado e indolor no leito. Após 15 sessões de fisioterapia, a paciente recebeu alta hospitalar. **Conclusão:** O uso da fotobiomodulação se mostrou eficaz para o tratamento complementar da fase aguda da síndrome de Stevens-Johnson no que diz respeito à regeneração tecidual e analgesia. **Palavras-chave:** síndrome de Stevens-Johnson; terapia por luz de baixa intensidade; neoplasias da mama; especialidade de fisioterapia.

RESUMEN

Introducción: El síndrome de Stevens-Johnson es una condición rara y potencialmente fatal que requiere diagnóstico temprano y tratamiento adecuado para asegurar un buen pronóstico. Debido a la complejidad del síndrome y la falta de un tratamiento estándar de las heridas, se ha discutido el uso de fotobiomodulación. **Informe del caso:** Mujer, 30 años, con cáncer de mama metastático, portadora de los síndromes de Stevens-Johnson y Li-Fraumeni Like en uso de la fotobiomodulación como estrategia adyuvante para el tratamiento del dolor y las heridas cutáneas. Las heridas cutáneas eritematosas comprometían casi toda la superficie corporal, con lesiones dolorosas, descamativas, crostosas y ampollas, con puntos hemorrágicos en la región posterior de ambos lóbulos de las orejas y en la región occipital, que dificultaban la acomodación del paciente en decúbito lateral y en posición cómoda semirreclinada. Se realizaron dos aplicaciones de fotobiomodulación (rojo, con longitud de onda de 660 nm) en región occipital y auricular con dosis de 2 Joules por punto; y 4 Joules en la región escapular para analgesia (infrarrojo, con longitud de onda de 808 nm). Ambas aplicaciones fueron seguidas de movilización y liberación miofascial en la región escapular. En 48 horas hubo una regresión de las lesiones cutáneas y mejoría del dolor, lo que facilitó una adecuada e indolora posición en la cama. Después de 15 sesiones de fisioterapia, la paciente fue dada de alta del hospital. **Conclusión:** El uso de la fotobiomodulación demostró ser efectivo para el tratamiento complementario de la fase aguda del síndrome de Stevens-Johnson en lo que respecta a la regeneración tisular y la analgesia. **Palabras clave:** síndrome de Stevens-Johnson; terapia por luz de baja intensidad; neoplasias de la mama; especialidad de fisioterapia.

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INTRODUCTION

Stevens-Johnson syndrome (SJS) is a severe, potentially fatal condition¹ that requires early diagnosis and appropriate treatment to ensure a good prognosis for the patient². With an annual incidence of one to two cases per million people and mortality of 1% to 9%³, sepsis is the main cause of death². Its manifestation involves malaise and fever, evolving with painful skin and mucous membrane lesions (ocular, oral and genital) that are characterized by disseminated erythematous rash⁴. Lesions can increase in size and number, coalesce, and the skin can totally detach^{3,5}, favoring the risk of infection and altering the affected structure.

Hypersensitivity mediated by immune complexes and triggered by drugs, viral infections and neoplasms is the main characteristic of SJS¹. This makes the cancer patient more susceptible to the development of the syndrome, as cancer and drug therapy are important triggers of this condition¹. Comorbidities, advanced age, genetic susceptibility, and immune diseases are predisposing factors. Aromatic anticonvulsants, allopurinol, and antibiotics, especially sulfonamides, are the most common causes of SJS¹.

There is no established treatment protocol, but it is known that the performance of a multidisciplinary team can increase survival³. Treatment includes withdrawal of the causative drug, suppressive therapy, intensive support, information communication and emotional support¹.

In this sense, photobiomodulation (FBM) can contribute to improving dermatological lesions and pain resulting from SJS. Analgesic effects, tissue regeneration and modulation of the inflammatory process are established in the literature for application in various conditions^{6,7}, including oncological conditions⁸.

Although the studies included in systematic reviews⁹⁻¹¹ on the use of BMF in cancer patients have a positive outcome for complications of radiotherapy and chemotherapy, there is divergence between the respective methodologies. These reviews indicate lack of information on parameters used and diversity of protocols⁹, insufficient data and low quality of evidence¹⁰, and studies with short follow-up time¹¹, thus limiting the recommendation for the use of FBM in clinical oncology practice.

Due to the complexity of SJS associated with the oncological condition and the lack of a standard treatment, FBM has been discussed in this condition.

This project was submitted to the Research Ethics Committee of the Faculty of Medical Sciences, of the State University of Campinas (UNICAMP), and approved with opinion n°. 6.109.618 (CAAE: 69233923.0.0000.5404), in compliance with Resolution 466/12¹² of the National

Health Council for research with human beings. The Committee was justified in waiving the signing of the Informed Consent Form.

CASE REPORT

Woman, 30 years old, diagnosed in 2017 with breast cancer and followed at the Center for Integral Attention to Women's Health (CAISM) at UNICAMP. At this time, genetic sequencing was performed, proving the presence of Li-Fraumeni Like syndrome, an autosomal dominant condition predisposing to several malignant tumors at an early age. The syndrome is associated with abnormalities in the TP53 gene encoding the tumor protein p53¹³.

Neoadjuvant chemotherapy was indicated as an oncological treatment – four cycles of adriamycin and cyclophosphamide, and 11 cycles of carbocitabine and taxol. In June 2018, the patient underwent right mastectomy with skin preservation, sentinel lymph node biopsy and dermoexpander implantation, with no indication of adjuvant therapy.

In March 2019, during preoperative examinations for the second time of breast reconstruction, bone (skullcap and middle third of the right femur), visceral (liver and lung), lymph node, subcutaneous tissue, contralateral breast, and central nervous system (CNS) metastasis was diagnosed, and palliative radiotherapy for CNS and chemotherapy with capecitabine were indicated.

The following month, the patient returned to the hospital referring a seizure, and phenytoin was prescribed. In May 2019, he returned to CAISM with signs and symptoms characteristic of SJS, probably secondary to phenytoin. In addition to the dermatological changes, dyspnea and acute pain were observed on the lower edge of the right scapula. After dermatological and ophthalmic evaluation, the diagnosis of SJS was confirmed. Phenytoin was replaced by valproic acid and ocular hydration was indicated due to keratoconjunctivitis. Erythematous skin lesions involved almost the entire body surface. Crusty, bullous scaly lesions with bleeding and very painful spots appeared in the occipital and posterior regions of the earlobe (Figure 1, A and B, respectively), making it difficult to position in the dorsal and lateral decubitus, and in the semi-reclined position.

As a therapeutic choice for tissue repair of the ear and occipital regions, the CAISM physiotherapy team chose to use portable FBM (DMC® brand), with 100 MW of power and *spot size* of 0.03 cm², and the parameters: 2 Joules per application point with a red wavelength of 660 nm; and, for analgesia in the scapular region, 4 Joules with an infrared wavelength of 808 nm. Two applications were performed with an interval of 24 hours and exercises in

small amplitudes for shoulders, scapular mobilization and myofascial release were performed in both sessions.

After 48 hours of these conducts, there was regression of skin lesions (Figure 1, C and D), decreased pain, and comfort during decubitus changes, according to the patient's report. Simultaneously with physiotherapy, cyclosporine was discontinued. However, the patient remained hospitalized for oncological, ophthalmological and physiotherapeutic follow-up. After 16 days of hospitalization and 15 physiotherapy sessions, the patient was discharged with guidance to return to the respective areas.



Figure 1. Occipital lesions (A); posterior earlobe (B); before and after two FBM applications (C and D)

DISCUSSION

The management of SJS symptoms during the acute phase is complex and the combination of different therapies appears to be effective. However, the standard treatment is not yet established^{3,5}.

FBM in the tissue repair process has scientific evidence and the most accepted mechanism of action is based on mitochondrial photoceptor, cytochrome C oxidase and chromophores in the plasma membrane of cells. The interaction of the wavelength in the red spectrum with the photoceptor triggers cell signaling pathways, altering cell metabolism and its proliferation¹⁴.

Studies related to SJS associated with FBM for the control of acute skin lesions were found in the literature, demonstrating that this resource can accelerate tissue repair, relieve pain, reduce complications and improve quality of life^{15,16}. Simões et al.¹⁶ described positive results for analgesia and healing in a pediatric patient with SJS, corroborating Rocha et al.¹⁷, who used FBM in oral mucosa with red wavelength and found a positive outcome. The study by Broughton et al.¹⁸ demonstrates that FBM accelerates the acute phase of inflammation, stimulates cell proliferation, increases skin wound contraction, and accelerates re-epithelialization, promoting tissue regeneration.

In oncological cases, FBM has been used to manage symptoms resulting from treatment toxicity such as oral mucositis, lymphedema, radiodermatitis and

chemotherapy-induced peripheral neuropathy. However, the challenge is to know whether or not there is growth of remaining tumor cells from the stimulus promoted by the light, increasing the risk of recurrence or development of a second primary tumor¹¹.

The results of a randomized, controlled and cross-sectional experimental study¹⁹ were analyzed, with groups of rats with induced breast cancer, followed by mastectomy, application of transcutaneous electrical nerve stimulation (TENS), interferential current or FBM in the region of the surgical wound. It was found that, in the FBM group, there was no tumor recurrence, unlike the result found for TENS and interferential current. In another study²⁰, which evaluated the safety of FBM applied to the head of patients with head and neck cancer, the development of tumor recurrences and/or new primary tumors was also not observed.

However, in a systematic review¹¹ on oncological safety and FBM in the prevention and/or treatment of complications related to antineoplastic therapy (oral mucositis, radiodermatitis, lymphedema and chemotherapy-induced peripheral neuropathy), the authors suggest that its use is safe, but conclude that studies with similar FBM application protocols and long-term follow-up are necessary to confirm oncological safety. For these authors, the follow-up time of less than two years can be considered a relevant limiting factor when it comes to malignant neoplasm¹¹.

In view of the lack of consensus in the literature regarding BMF and oncological safety, in addition to Li-Fraumeni Like Syndrome, the physiotherapy team thoroughly discussed whether this resource should be applied to skin lesions and the painful region. The physical and emotional conditions in which the patient found herself – with multiple metastases, suffering resulting from pain in the lesions, difficulty in movement and impaired sleep – strongly contributed to the decision to use FBM. The significant improvement in symptoms in 48 hours, with discharge of the patient by the dermatology team, had a positive outcome for this case.

CONCLUSION

Due to the lack of consensus in the literature on the use of FBM in oncological situations, the professionals involved should discuss and consider potential risks and benefits to patients. For this case, FBM was effective as a complementary treatment in relation to tissue regeneration and analgesia, promoting improvement to the patient. More robust studies should be carried out to better understand FBM in oncological conditions, allowing advances in the definition of parameters with safety.

CONTRIBUTIONS

All authors contributed substantially in the design and/or planning of the study; in the collection, analysis and interpretation of data; in the writing and critical review; and approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

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