Advanced non-small cell lung cancer associated with hemophagocytic syndrome in a cachectic patient

It is generally known that some viral infections, autoimmune diseases and hematologic malignancies, such as malignant lymphoma, can cause hemophagocytic syndrome (HPS). In contrast, non-hematologic malignancies associated with HPS have rarely been reported. A case of malignancy-associated hemophagocytic syndrome (MAHS) by non-small cell lung cancer in a cachectic patient to our knowledge has never been reported. Thus, this is the first reported case of MAHS in a lung cancer patient with cachexia syndrome.

A 56-year old man had presented with the chief complaint of high fever and general fatigue for 2 days prior to being referred to us. He has a history of rheumatic arthritis for which had not required any medication. He had stage IV (cT4N3M1, BRA) non-small cell lung cancer (adenocarcinoma) in a cachectic state (body mass index = 17.7 kg/m²) and had received chemotherapy of pemetrexed alone for 2 weeks.

An empirical intravenous therapy of tazobactam/piperacillin was begun for febrile neutropenia because bicytopenia appeared (leukocytes = 3 x 10³/µL; hemoglobin = 9.1 g/dL; platelets = 171 x 10⁹/L). All viral antigen tests including flu, sputum and blood cultures were negative and chest radiography showed no abnormality except for cancer tumor shadow. Seven days after admission, he had fever associated with pancytopenia (leukocytes = 2.4 x 10³/µL; hemoglobin = 8.9 g/dL; platelets = 83 x 10⁹/L) without any other related symptoms. A bone marrow biopsy revealed HPS (Figure 1) and he was diagnosed as HPS associated with lung cancer. No evidence of cancer metastasis was seen in the bone marrow. Dexamethasone was administered intravenously for 4 days and the pancytopenia improved. As a result the lung cancer progressed and respiratory failure developed. He died on day 28.

While malignant lymphomas associated with HPS have been sporadically demonstrated, secondary HPS caused by non-hematologic malignancies is extremely rare. The pathophysiological mechanism for HPS is still unknown. Some authors have demonstrated that HPS is associated with the release of large numbers of cytokines; cytokine storm. Also, it has previously been described that the level of cytokines such as IL-6 or TNF-α is high in patients with cancer cachexia. Since cytokine storm may be related to the origin of HPS, we can presume that cachectic cancer patients might be at risk for HPS. For clinicians, except for hematologists, HPS is not so common and thus might unfortunately be overlooked. Since pancytopenia can be lethal, it should be cautiously monitored. HPS may possibly develop to disseminated intravascular coagulation and multiple organ dysfunction.

Figure 1 – Bone marrow smear showing macrophages with hemophagocytosis
Low-level laser therapy of leg ulcer in sickle cell anemia

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Chronic leg ulceration affects about 1% of the population at some point in their lives. Additionally, leg ulcers are one of the sequels of sickle cell disease with physiological and psychosocial consequences. Treatment aims at improving the quality of life of patients and effectively healing the lesion. Adherence to treatment is not always effective, especially considering the profession of individuals with sickle cell anemia and the time required for therapy. The results of current therapeutic conduct appear to be unsatisfactory even though much has been published on a wide range of therapies.

Cutaneous lesions represent a dilemma and instigate clinical interest because of the high morbidity associated with changes in the normal healing process. An adequate choice of therapy and effort of the medical team can make the healing process quicker and reduce possible complications.

Among currently available methods, low-level laser therapy (LLLT) is an important, safe and practical tool. In vitro and in vivo studies have demonstrated that LLLT is an effective method to modulate tissue repair, thus significantly contributing to a faster and better organized healing process.

Here we describe the results of a therapeutic intervention in a 35-year-old female sickle cell anemia patient with recurring leg ulcers who was prevented from maintaining employment and appropriate social activities due to the disease. She had been diagnosed at 8 years old; she is homozygous for the Bantu haplotype. Between 16 and 18 years old, the patient was repeatedly hospitalized for infections, leg ulcers, generalized pain and anemia. Leg ulcers were a recurring problem which affected daily-to-day activities.

The patient participated in the "ulcer healing group" of Hospital de Base in São José do Rio Preto, São Paulo State, Brazil and the leg ulcers were treated. At an initial evaluation the patient had an active leg ulcer of the lower third of left leg above the medial malleolus. She also had whitish areas in the third anteromedial distal region of the left leg and on the dorsum of the foot, showing that several ulcers had healed. A macroscopic evaluation identified the presence of hyperpigmentation and the temperature in the region was elevated.

Treatment using LLLT was proposed to accelerate the healing of the ulcer. The device used was a He-Ne Laser (Plasmax IV - KLD Biosystems Inc.) with a wavelength of 632.8 nm and red (visible), 5mW peak emission, 10 - 60 mJ energy with an application area of 0.02 - 100 cm² and automatic dosimeter.

The application mode consisted of point action of 30 mJ for 9 seconds in order to accelerate local cell stimulation for healing. Points at 5 - 10 mm intervals on the edges of the ulcer were marked and laser therapy was applied. Moreover, with the aim of increasing circulation, 50 mJ were applied for 15 seconds in the region above the ulcer. A total of five treatment sessions were used twice weekly for 10 to 15 minutes each with progressive reduction as the ulcer healed.

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