LETTER TO EDITOR

Musculoskeletal manifestations in patients with post-COVID-19 syndrome: key aspects

Manifestaciones osteomusculares en el paciente con síndrome post-COVID-19: aspectos claves

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To Editor:

The global health contingency generated by SARS-CoV-2 has caused clinical repercussions in patients both in the acute phase and in the convalescence phase of the disease, which can last up to the first three months, generating the post-COVID-19 syndrome (PCS). The latter should be considered in the clinical approach of all patients who have had the disease, as it represents a heterogeneous group of clinical manifestations and/or disorders that cover a wide variety of signs and symptoms, ranging from innocuous and nonspecific respiratory symptoms to manifestations that occur in different systems with specific behaviors of each one. PCS represents more particularly frequent and serious behaviors in those patients who have stayed in hospitalization areas and intensive care units[(1)].

Musculoskeletal manifestations are an interesting topic in PCS, as it has been observed that patients who had a moderate to severe degree of infection tend to maintain a substantial musculoskeletal burden of the disease, consequently generating greater disability secondary to skeletal, neurological, muscular, and articular disorders. Greater osteomuscular impact was associated with fatigue in patients with prolonged ventilation states secondary to pro-inflammatory states. These proinflammatory states are mediated by a variety of cytokines such as Chemokine 10 with C-X-C Ligand Factor (CXCL10), Interferon Gamma (IFN-g), Interleukin 1 beta (IL-1b), Interleukin (IL-6), Interleukin 8 (IL-8), Interleukin 17 (IL-17), and Tumor Necrosis Factor alpha (TNF-a). In addition, the overexpression of angiotensin-converting enzyme 2 (ACE-2) and serine protease transmembrane protease, TMPRSS2, receptors in some tissues such as the synovial membrane and muscle tissue, are expressed together in lung tissue, generating a chemotactic response through the cytokines previously mentioned, generating the overaggregation of different defense cells (B Lymphocytes, Macrophages, and NK cells), which induce an immune-mediated response that results in deleterious effects such as muscle and bone fragility, negatively impacting the quality of life and prognosis of patients[(2–4)] (Figure 1).

The muscular system presents symptoms associated with myalgia and generalized weakness, the latter of which has shown great significance in the progression of the disease overall, as demonstrated in a study conducted by Mao L et al in 1929 symptomatic patients infected with SARS-CoV-2, which evaluated CK (creatine kinase) values in relation to the presence of the disease. It was found that in patients with values above the threshold who also experienced neurological outcomes related to motor control and muscle strength alterations in approximately 36% of the participants, such outcomes were associated with physical deconditioning states produced during the recovery period or SPC state[(6)]. In some studies conducted in post-mortem patients, generalized muscle atrophy associated with sporadic and focal necrosis of these fibers and infiltration of pro-inflammatory cells, as well as disorganization of myofibrils and alterations in Z disks, which are crucial for force transmission, have been observed[(7)].

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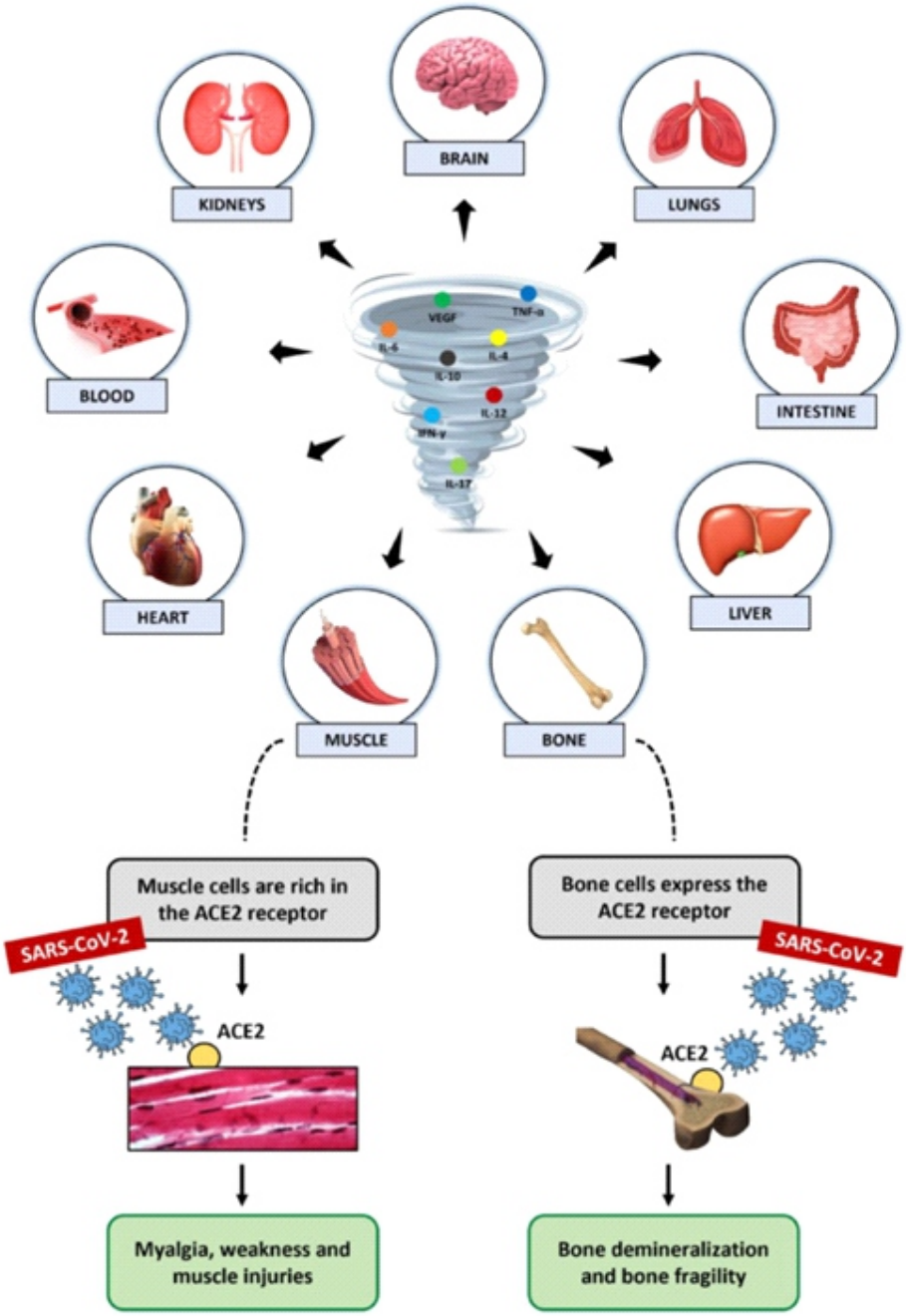

Figure 1. Pathophysiological diagram mediated by cytokine cascade with osteomuscular implications osteomusculares[5]

Osteoarticular findings are less described in relation to muscular findings throughout the literature, as changes associated with arthralgia, such as lower bone mineral density, are mainly described at this level and are largely indirectly associated with steroid treatment used to treat patients with moderate to severe infection. In the latter group of patients, changes associated with osteonecrosis have been described with higher frequencies primarily in anatomical areas such as the femoral head, knee, humeral head, talus, and calcaneus. These osteonecrosis findings could be related to hypercoagulability states secondary to alterations in microvascular flow generated by leukocyte aggregation and chronic inflammation in SPC states[8].

The aforementioned osteomuscular findings reflect multiple changes in SPC states related to conditions of sarcopenia and osteoporosis, which make early implementation of rehabilitation strategies necessary in different patients in early stages of SPC, as early rehabilitation reflects greater recovery of osteomuscular system functionality[9]. Immunotherapy management was not discussed as they are still subject to studies in proximity.

Author´s contribution

All authors have contributed in the conception, drafting of the final manuscript, revision and approval of the manuscript.

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