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Leprosy and the scenery of COVID-19

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Abstract
The potentially negative consequences of COVID-19 in the routine assistance of leprosy patients should merit special attention of the health and political authorities in underdeveloped regions with a higher prevalence of the ancient mycobacterial infection. Effective strategies are needed to protect patients and maintain the control of leprosy, while the preventive health public measures against COVID-19 are strictly followed. Pathophysiological mechanisms can be shared by leprosy and SARS-Cov 2 infection. Actually, either old or new infectious diseases should deserve enough attention by health workers, mainly whether the same population group is more prone to be affected.

Keywords: Covid-19, hanseniasis, leprosy, sars-cov2

Introduction

Leprosy is a chronic infection prevalent in low- and middle-income populations for more than 2,000 years, and currently coexisting with the COVID-19 pandemic [1-10]. Such interaction raised concerns about development of possible adverse consequences, and several authors have commented on some similarities and major potential risks. Current advent of a severe viral pandemic increased the burden on the public health system with priority for attention to patients with acute illness of high mortality rate. This short analysis aims to enhance the interest of health workers on the novel concerns.

Material and Methods

The commentaries were carried out based on some recent publications of high indexing level (Pubmed), and major focus on the concomitance of COVID-19 with leprosy. The main searched disturbances included: respiratory invasion pathway and hyposmia or anosmia; pro-inflammatory factors and cytokine storm; Th2 response and severe organ damage; development of neutrophilia; risk of the silent neuropathy; and risk or benefits of drugs utilized to treat leprosy or the viral infection.

Dear Editor,

Leprosy may involve immunological, genetic, nutritional, and environmental factors [5]. Although treated with rifampicin, clofazimine, and dapsone for 6 to 12 months, leprosy patients can have immune-mediated reactions with nerve damage and high mortality [3, 5]. Clofazimine, dapsone, nor BCG vaccine have an effect on the COVID-19 severity [4, 7]. In leprosy, the nasal mucosa is the invasion pathway, and the mycobacteria infect the olfactory structures, early causing dysfunctions like hyposmia and anosmia; many of the COVID-19 patients have had similar disturbances due to the virus neurotropism [1, 2, 5]. The cytokine storm characterized by high levels of interferon-γ, tumor necrosis factor, interleukins, and chemokines is frequently described in severe forms of COVID-19; worthy of note the proinflammatory factors are also elevated in leprosy reactions [1, 2, 7, 10]. *Mycobacterium leprae* elicits a Th1 and Th17 response preventing the multiplication of the agent (tuberculoid) and Th2 response that allows dissemination (lepromatous) [1, 2, 5]. Type IV hypersensitivity reaction causes a change from Th2 to Th1 resulting in Type-1 leprosy reaction (T1LR), while a type III hypersensitivity reaction leads to Type-2 leprosy reaction (T2LR) [2, 9]. T2LR occurs in lepromatous (15.4%) and borderline lepromatous (4.1%) leprosy; and infections are known as trigger factors for T2LR [5, 9]. Similar to leprosy, COVID-19 can develop a variable inter-individual response; some patients have elevated proinflammatory cytokines and chemokines and intense initial Th1 response against the virus, that elicits a Th2 response and severe organ damage [2]. During the T2LR, or erythema *nodosum leprosum* (ENL), typically occur diffuse or deep skin erythematous nodules and papules, and elevated levels of LDH can develop neutrophilia that theoretically propitiate a higher risk for severe COVID-19; while extracutaneous manifestations as malaise, fever, or arthralgia mimic this virosis [1, 5, 8]. Blood samples should be taken to evaluate the levels of interferon (INF-γ), interleukins (IL-10, IL-1β, IL-8, IL-6, and IL-12p70) and tumor necrosis factor-alpha (TNF-α) [7]. Borderline tuberculoid leprosy has developed after use of IL-6 inhibitor (tocilizumab); then, this IL-6R monoclonal antibody-directed must be avoided to treat COVID-19[1,8]. This drug should be cautiously used in leprosy-endemic areas during this pandemic.[1] IL-6 is related to leprosy reactions and also a marker of the neuropathic pain; hence, the co-infections leprosy and COVID-19 can be under a greater risk for silent neuropathy; the IL-12B gene expression was also found increased in patients with co-infection [4, 7]. ENL is a serious immunological complication affecting up to 40% of multibacillary patients, and requires the administration of oral corticosteroids and/or thalidomide [5]; some clinical trials utilize corticosteroid or thalidomide to treat COVID-19 patients [2, 10]. Systemic corticosteroids as prednisone ≥ 20 mg daily increase the risk of COVID-19, but the treatment with steroids in immunosuppressive doses can control a severe ENL [1]. Few cases of chronic ENL need long steroid use and the benefits of continuing the drug

outweigh the risk of azathioprine, methotrexate, and cyclosporine in COVID-19 [8]. Methotrexate and steroids used in severe ENL plus COVID-19 had a good outcome; high levels of INF-γ in leprosy may result in a favorable effect on this viral infection [9]. T2LR is associated with an inflammatory response INF-γ mediated, a cytokine that can play a role in the clearance of SARS-CoV-2 and protect against a severe COVID-19 [9]. Epidemics lead to impacts on the routine of the public health systems; some measures may create barriers to the access of patients and/ or reduction of leprosy care services; this would result in additional delays in the diagnosis of leprosy and its complications [3]. So, there was a reduction of 44.4% in the leprosy diagnosis comparing 2019 and 2020; and 24.25% fewer municipality reporting of cases: 251 in 2019 and 202 in 2020 [6]. Cerqueira *et al*., assessed the influence of leprosy-related variables in the occurrence and severity of COVID-19 in a 14-month study. Among the 406 included patients, 113 had diagnosis of leprosy; and in follow-up 69 (16.99%) contracted the COVID-19 [4]. Only household contacts COVID-19-positive and diabetes were significant risk factors. At least in part, leprosy patients are susceptible to COVID-19 due to more frequent contact with infected people, because of shared poorer social and economic situations [4]. Morais Junior *et al*. evaluate data of 114 individuals; 64 with leprosy (before, during, and up to three years after polychemotherapy), and 50 controls without leprosy [7]. Twelve leprosy patients (mean time since the onset of COVID-19, 43.54 days; range: 6-75 days) and 14 non-leprosy patients (mean time since the onset of COVID-19, 41.84 days; range: 6-90 days) diagnosed with COVID-19 by the reverse-transcriptase PCR [7]. Cytokine levels measured were higher in patients who contracted COVID-19 than in leprosy patients and controls, even at more than 30 days after the onset of COVID-19; results suggesting that inflammation in COVID-19 can stimulate the leprosy reactions [7].

Conclusion

The included comments may enhance the awareness of health workers about possible adverse interactions between concomitant COVID-19 and leprosy, mainly in middle- and low-income regions with unsolved or neglected problems of public health. Only more follow-ups of coexistent leprosy and COVID-19 will allow specialists to get a consistent conclusion on the pathophysiological action of one infection over the other.

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