

Cutaneous Hyperesthesia Associated with Covid-19: Case Report

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Abstract:

Introduction: Cutaneous hyperesthesia is a neurological symptom that manifests itself as exacerbated sensitivity in the skin. This symptom has been shown to be present in a small percentage of cases of patients with Covid-19; however, research has yet to demonstrate its relationship to prognosis. Treatment is multimodal in nature, ranging from expectant conduct to psychological approach associated with physical methods, use of antidepressants or anticonvulsants and surgery, if there is no spontaneous resolution after the disease is cured.

Case report: A 48-year-old male patient presented with significant rhinorrhea and cutaneous hyperesthesia on the back after having contact with a confirmed case of Covid-19; when performing the exam on the fourth day of symptoms he tested positive for SARS-Cov-2 infection.

Discussion: Mild and transient neurological complications are present in up to 91% of patients with Covid-19; unusual complications, such as sensory deficits, affect only 0.2 to 1.4% of those infected. The hypotheses studied so far, to explain the ways in which the virus enters the central nervous system (CNS), involve blood dissemination and neuronal transport. Although there are studies that show the relationship between neurological manifestations and a worse prognosis in patients with Covid-19, a direct relationship between cutaneous hyperesthesia and unfavorable evolution has not been found so far in patients infected with SARS-Cov-2.

Conclusion: In view of the wide variation in the presentation of SARS-Cov-2 infection and considering the current epidemiological situation of the pandemic, the possibility of infection by the new coronavirus should be considered in the definition of differential diagnoses associated with cutaneous hyperesthesia, in order to avoid delay in adoption of surveillance measures and containment of the spread of the new coronavirus.

Keyword: Coronavirus Infections; Hyperesthesia; Skin Abnormalities.

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I. Introduction

SARS -CoV-2 can cause severe and even life-threatening respiratory problems (LI *et al.*, 2020). However, the complications caused by Covid-19, a disease that has killed more than 2 million people worldwide, are not limited to the lungs, but can cause damage to other body systems. Although rare and little discussed, cutaneous hyperesthesia has already been reported as a complication of Covid-19 (KRAJEWSKI; SZEPIETOWKI; MAJ, 2020). Such pathology is defined by the International Association for the Study of Pain as increased sensitivity to stimulation (IASP, 2010). The pathophysiology of this manifestation is based on damage to the central nervous system (CNS) and / or peripheral nerves, but the mechanism by which SARS-Cov-2 triggers hyperesthesia has not yet been clarified. The participation of the angiotensin-converting enzyme receptor 2 (ACE2) and the Sars-CoV-2 peak protein, in addition to the invasion of the peripheral nerve by the virus, are possible hypotheses to explain this symptom (KRAJEWSKI; MAJ; SZEPIETOWKI, 2020).

II. Case Presentation

White male patient, 48 years old, doctor. He started with a severe rhinorrhea accompanied by intense cutaneous hyperesthesia on his back, which worsened throughout the day and relieved only with cold baths. At night, the sensation worsened and interfered with the quality of sleep. He denies fever or cough. Pulmonary auscultation without changes. The patient reports having examined an elderly person with suspected Covid 19 about four days before the onset of symptoms and having collected a nasal swab to confirm the diagnosis of the elderly person without the use of adequate personal protective equipment. The patient underwent RT PCR for Covid 19 in a nasal swab, on the fourth day of symptoms, with a positive result. Blood count, liver function,

kidney function, D-dimer and C-reactive protein were also collected, which did not show significant changes. He progressed well, with rhinorrhea improvement in the following days and partial remission of cutaneous hyperesthesia on the back after six days of illness, without using any medication. Even after 60 days of the initial condition, the patient reports maintaining the sensation of cutaneous hyperesthesia on hot days, with relief after ingestion of cold liquids or bathing.

III. Discussion

Mild and transient neurological complications such as dizziness, anosmia, dysgeusia, headache, altered level of consciousness and agitation are frequently reported in patients infected with Covid-19, with a case series reporting such symptoms in almost 91% of patients (KRAJEWSKI; MAJ; SZEPIETOWKI, 2020). There is evidence that such changes occur due to the direct invasion of Sars-CoV-2 in the CNS, producing tissue damage that generates mild neurological disorders (KORALNIK; KENNETH, 2020), and, to a lesser extent, serious complications, such as ischemic and / or hemorrhagic stroke and encephalopathy. A study carried out in Chicago, with 509 patients who tested positive for Covid-19, showed that 0.2 to 1.4% of the cases presented neurological symptoms considered unusual, among them sensory deficits (LIOTTA *et al.*, 2020).

Experimental evidence in animals shows that the coronavirus present in lung tissue can reach the brain through the bloodstream (YAVARPOUR-BALI; GHASEMI-KASMAN, 2020). Another way of accessing the CNS would be by axonal transport and transneuronal dissemination of olfactory and trigeminal nerve endings in the nasal epithelium (ROMAN *et al.*, 2020). This neuronal invasion can occur through retrograde and anterograde transport along peripheral nerves. The olfactory bulb, for example, can be entered through TMPRSS2 and ECA2 receptors or through extracellular vesicles present in olfactory sheath cells, which do not depend on ACE2 receptors (YAVARPOUR-BALI; GHASEMI-KASMAN, 2020).

The virus can also be transported to the brain tissue via trigeminal and vagus nerves, which may be related to respiratory failure present in Covid-19, since the cardiorespiratory center present in the brain stem is also innervated by these cranial pairs. Another way for the virus to enter the CNS is the bloodstream itself, through the infection of the blood-brain barrier epithelial cells in the choroid plexus of the cerebral ventricles (YAVARPOUR-BALI; GHASEMI-KASMAN, 2020). On the one hand, infection by SARS-COV-2 leads to pneumonia and impairment of the cardiorespiratory regulation center of the brain stem, which leads to hypoxia. On the other hand, hypoxia exacerbates neural damage leading to a deadly vicious cycle. These findings support the higher prevalence of neurological symptoms in critically ill patients (NIAZKAR *et al.*, 2020).

Although the mechanism of neuronal invasion of SARS-Cov-2 is already partially known, the pathophysiology of cutaneous hyperesthesia as an isolated neurological manifestation in patients who evolve without major respiratory impairment has not been completely clarified. One of the studies that investigates this issue points to the possibility of injury to the multifocal peripheral nervous system or peripheral polyneuropathy associated with inflammation triggered by the virus as possible pathophysiological mechanisms associated with hyperesthesia. In these cases, there would be a change in conduction via the paleo-spinothalamic route, in the dorsal horns in the spinal cord, with involvement of the C fibers in the area affected by hypersensitivity (HADLEY *et al.*, 2016). C fibers are responsible for the transmission of thermal, mechanical and chemical stimuli, lead to pain of the slow type and are located in deeper structures of muscles, tendons and viscera. The stimulus is conducted without precise somatotopic organization and, therefore, the pain transmitted by them is difficult to locate and quantify. This mechanism and a semiological manifestation similar to what occurs in patients infected with the herpes virus, which may favor the hypothesis of the intrinsic neurotropism of SARSCoV-2, defended by several researchers. (LIGUORI *et al.*, 2020 and YAMADA *et al.*, 2019).

Another hypothesis to explain cutaneous hyperesthesia discusses the role of angiotensin-converting enzyme (ACE2) receptors as one of the possible ports of entry for Covid-19 in the cells of the nervous system related to sensitivity, since the tropism of the virus by these receptors, present on the surface of other cells, has been widely confirmed (KRAJEWSKI; MAJ; SZEPIETOWSKI, 2020). This pattern of alteration in painful sensitivity would occur due to the reorganization of sensory transmission within the nervous system after nerve injury, either by direct injury to the virus or by intense local inflammation secondary to the injury. The reorganization would include changes in the expression of neurotransmitters, neuromodulators, receptors, ion channels and structural proteins (HUDSPITH *et al.*, 2006).

Common characteristics found in our patient and in other patients analyzed by two studies (KORALNIK; KENNETH., 2020 and HARSCH, 2021) were a major discomfort in the posterior thoracic region, relief with hot baths and progressive improvement after one week of infection, without the use of specific medications.

Although there are studies showing the relationship between neurological manifestations and encephalopathies with a worse prognosis in patients with Covid-19, so far, no direct relationship has been found between cutaneous hyperesthesia and unfavorable outcome in patients infected with SARS-Cov-2. Given the

apparent rarity of this manifestation in patients infected with Covid-19, it is clear that further studies should be carried out in order to clarify the pathophysiological mechanisms of this manifestation, to elucidate the long-term effects of SARS-CoV-2 on sensitivity and especially to define the relationship of this symptom with the prognosis of the disease, since, in most cases in which hyperesthesia was associated with patients with laboratory confirmation of Covid-19 infection, there was an evolution to cure without complications.

IV. Conclusion

Cutaneous hyperesthesia is an uncommon manifestation that appears in the early stages of Covid-19 infection. Health professionals should be attentive to patients who present this complaint, as it is a non-specific symptom and still little associated with SARS-Cov-2. The current epidemiological situation must be considered when defining differential diagnoses associated with this sensitivity disorder in order to avoid incorrect diagnoses and delay in adopting surveillance measures and containing the spread of the new coronavirus.

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