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Review Article

Long COVID: A Diagnostic Methodology (An Observational Study)

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Abstract

Importance: Long COVID has been defined as a chronic medical condition that occurs after a SARS-CoV-2 infection and is present for at least three months [1-3]. Long COVID includes a wide range of symptoms or conditions that may improve, worsen or to be ongoing, per criteria published by the Centers for Disease Control and Prevention. However, criteria confirming the diagnosis has yet to be developed. Several others have, though, identified a clinical overlap between Long COVID and fibromyalgia [4-10]. Their theories, however, lacked any objective documentation for the existence of fibromyalgia and therefore, the use of a well-established diagnostic fibromyalgia blood test was the basis for analyzing a cohort of patients with Long COVID.

Objective: To determine whether Long COVID infections could be objectively diagnosed via a blood test based upon the shared and proven characteristics between Long COVID and fibromyalgia.

Design, setting and participants: This cohort study recruited individuals who historically were diagnosed to have Long COVID based upon evidence of a past COVID-19 infection and related persistent symptoms. None of the individuals had experienced previous similar symptoms prior to the onset of their COVID-19 infection. Each individual had only experienced a single COVID-19 infection.

We recruited test-positive SARS-CoV-2 patients who had no chronic medical complaints prior to the onset of this infection and who post-SARS-CoV-2 had at least a 6 month history of chronic medical complaints, the nature of which have been recognized as common manifestations which define a Long COVID medical status. Those manifestations also classically define what afflicts fibromyalgia patients. The latter relationship has been recognized by multiple other researchers. These patient volunteers underwent blood testing for established immune system biomarkers which document and confirm the diagnosis of fibromyalgia.

Main outcomes and measures: A total patient population of 21 individuals was recruited. An analysis via blood testing looking for established criteria for the diagnosis of fibromyalgia which included peripheral blood mononuclear cell related deficiencies regarding the chemokines and cytokines of MIP-1alpha, MIP-1beta, IL-6 and IL-8 of all of the patients documented that 18 now had evidence of these fibromyalgia diagnostic criteria.

Results: Clinical data regarding 21 volunteers was obtained to confirm their development of a SARS-CoV-2 infection. They were individually interviewed and they completed related health questionnaires. All volunteers had evidence of a positive COVID-19 test score. All of the volunteers denied having a pre-existing background of similar symptoms. The volunteers were 13 females and 8 males. The symptoms reported were: Headaches (78%), Brain Fog (72%), Fatigue (67%), Depression/Anxiety (61%), Joint/Muscle Pain (50%), Sleep Disturbance (50%), Dizziness (44%).

Conclusions and relevance: A percentage of individuals who contract a COVID-19 infection will develop a "Long Haul" residual set of symptoms which they did not previously experience. These symptoms mirror a medical disease termed fibromyalgia, which is actually an immune deficiency medical disorder. Consequently, a recognized, peer-reviewed, highly sensitive and highly specific diagnostic fibromyalgia blood test was performed on these 21 Post COVID-19 infection individuals. Of this group, 18 (86%) tested positive for fibromyalgia. Therefore, a potential explanation for their persistent symptoms was objectively indentified and a potential origin of fibromyalgia was detected and linked to a Corona virus(es).

Introduction

The Sars-CoV-2 virus (COVID-19) induced a worldwide pandemic commencing in 2019. Though its primary manifestations concerned the human respiratory tract, significant and major immune system effects were also identified. A percentage of these patients went on to experience residual and persistent symptoms and rarely had there been a pre-existing nature of those medical complaints. According to the CDC Household Pulse Survey, those with these Long Haul traits can amount to 20% of those who developed a confirmed COVID-19 infection. The major symptoms the latter group reported included neurologic (brain fog, headaches, sleep problems, dizziness, depression or anxiety), fatigue, and joint or muscle pain. These symptoms are also classical manifestations of the medical disease known as fibromyalgia. However, no etiology of fibromyalgia has ever been identified, though estimates of the incidence of this medical condition are estimated to range as high as 6% of the population. Further, fibromyalgia has been reported in the medical literature for decades and long before the Corona virus of Sars-CoV-2 was known to exist.

We therefore decided to explore a potential set of relationships between Long Haul Post-COVID-19 patients and fibromyalgia patients. To do so, we relied on a peer-reviewed, highly sensitive and highly specific blood test which was developed by the Department of Pathology at the University of Illinois College of Medicine at Chicago. This test has been commercialized under the names of the FM/a® Test, the 100SURE Test and the BSURE Test.

We recruited a cohort of 21 Long Haul patients and they were screened not only for evidence of a previous COVID-19 infection but to also confirm the residual medical complaints they were experiencing. Our goals included whether there was an objective manner to document their persistent symptoms, to learn whether there could be a link to fibromyalgia and to explore the possible role of a human Corona virus in the origin of fibromyalgia.

Methods

Via multi-media, patients who had objective evidence of a previous COVID-19 infection and were experiencing the characteristics of Long Haul COVID in the Chicago, IL area were recruited. They were screened in-person to confirm that they met the latter criteria and were documented to have never had such symptoms on a prior basis. After receiving informed consents (UIC IRB), a total of 21 patient volunteers were identified. All then underwent the FM/a® Test diagnostic blood test to determine whether they had proof of fibromyalgia. The FM/a® test determines whether there are specific deficits in the chemokines and cytokines of MIP-1alpha, MIP-1beta, IL-6 and IL-8 [11,12]. All participants additionally were personally interviewed and they individually completed related health questionnaires.

Results

The volunteers were asked via their self-reporting questionnaires whether they were experiencing not merely established Long Haul COVID-19 symptoms but also whether they had any chronic or pre-existing medical complaints. All were over the age of 18. They consisted of 13 females and 8 males. All had persistent symptoms for 180 days or longer. The questionnaires listed these symptoms:

- Chronic Fatigue
- Brain Fog
- Anxiety/Nervousness Feeling Depressed
- Trouble Concentrating
- Headaches
- Restless Legs
- Poor Sleep
- Muscle/Joint Pain
- Leg Cramps
- Numbness
- Ringing of the ears
- Dizziness
- They reported symptoms of:
- Headaches 78%
- Brain Fog 72%
- Fatigue 67%
- Depression or Anxiety 61%
- Joint/Muscle Pain 50%
- Poor Sleep 50%
- Dizziness 44%
- Regarding the FM/a® Test results, 18/21 (86%) of the patients had a positive test score for fibromyalgia.

Discussion

Since the advent of the SARS-CoV-2 (COVID-19) pandemic, a significant percentage of these post-infectious patients have gone on to experience residual persistent symptoms. An objective source for these symptoms has avoided to be discovered. However, the classic post-COVID-19 (Long Haul) symptoms are essentially identical to those which have been attributed to the medical disease that has been labeled as fibromyalgia. Yet, the medical condition of fibromyalgia has been reported and diagnosed for many decades and long before COVID-19 infections were known to occur in humans.

We had particular interest in not merely potentially objectively identifying a basis for the persistence of the symptoms in Long Haul COVID-19 patients. We also desired to investigate if there was a source for why there was the development of fibromyalgia. We used multi-media sources to attract Long Haul COVID-19 patients whom we could document had experienced a COVID-19 infection, were willing to be personally interviewed, would complete related medical questionnaires and would also submit to undergo an established, highly sensitive and highly specific diagnostic blood test for fibromyalgia. While we secured such a cohort of volunteers, the number who were willing to meet all of these criteria proved limited.

Nevertheless, the findings were significant. Of the volunteers, 86% tested positive for fibromyalgia and for the related immune system deficiencies concerning the peripheral blood mononuclear reductions of the chemokine and cytokine proteins of MIP-1 alpha, MIP-1 beta, IL-6 and IL-8.

The origins of fibromyalgia have been debated for years. They have included hypothetical pathways stemming from trauma, emotional afflictions, post-surgical complications and chemical sensitivities among others. However, the only objective criteria that have ever been proven to exist in fibromyalgia is documentation that these individuals suffer with immune system deficiencies and in particular, an inability of their peripheral blood mononuclear cells to produce normal quantities of two chemokines, MIP-1 alpha, MIP-1 beta and two cytokines, IL-6 and IL-8.

Clearly, the extremely high percentage of Long Haul COVID-19 volunteers who tested positive for fibromyalgia far exceeds anything coincidental, circumstantial or fortuitous.

There are seven known human Corona viruses. Their role in being the leading origin of upper respiratory tract infections has been well-established.

Viruses can elicit epigenetic changes. According to recently published whole exome analyses, documentation of unique DNA pathways have been authenticated to occur in 100% of fibromyalgia/FM/a® test positive patients and in 0% of healthy, matched control patients [13].

It is our hope and desire to promote further investigations of Long Haul COVID-19 patients in sufficient quantity to verify the findings our initial investigation have detected and confirmed.

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