Case Report

Successful treatment with minocycline and Saiko-keishi-to for COVID-19-associated CNS lesion

Masashi Ohe*, Haruki Shida, Junya Yamamoto, Masahide Seki, Ken Furuya

Department of Internal Medicine, JCHO Hokkaido Hospital, Sapporo, Japan

*** Address correspondence to:**

Dr. Masashi Ohe

Department of Internal Medicine, JCHO Hokkaido Hospital

1-8-3-18 Nakanoshima, Toyohira-ku, Sapporo 062-8618, Japan

E-mail: oektsp1218@sweet.ocn.ne.jp

Tel: 81-11-831-5151

Fax: 81-11-821-3851

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Abstract

Neuropsychiatric manifestations of COVID-19 include delirium, general malaise, headache, and psychiatric symptoms. These manifestations are related to the neuroinflammatory response to viral antigens and proinflammatory mediators/immune cells. Tetracyclines, such as minocycline, have antibacterial and anti-inflammatory properties. Saiko-keishi-to, a traditional Japanese Kampo medicine, also has anti-inflammatory properties. Given the anti-inflammatory properties of minocycline and Saiko-keishi-to, we describe two cases of COVID-19 with prolonged headaches and general malaise successfully treated with these medications.

Keywords: COVID-19, minocycline, saiko-keishi-to

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Introduction

Coronavirus disease 2019 (COVID-19) is characterized by early exponential viral replication, cytokine-associated organ damage and dysfunction, endothelial injury with proximal platelet aggregation, and thrombosis (1).

Neuropsychiatric manifestations of COVID-19 include delirium, general malaise, headache, and psychiatric symptoms. These manifestations are related to the neuroinflammatory response to viral antigens and proinflammatory mediators/immune cells. In the central nervous system (CNS), the macrophage known as microglia cell mediates the excessive production of inflammatory cytokines, free radicals, and damage signals, which has neurotoxic effects (2).

Tetracyclines, such as minocycline, have antibacterial and anti-inflammatory properties (3). Saiko-keishi-to, a traditional Japanese Kampo medicine, also has anti-inflammatory properties (4).

Given the anti-inflammatory properties of minocycline and saiko-keishi-to, we describe two cases of COVID-19 with prolonged headaches and general malaise that were treated with these medications.

Case 1

A 42-year-old woman was taken to our hospital with symptoms of fever, sore throat, headache, and general malaise. She was diagnosed as having mild COVID-19 based on a positive polymerase chain reaction (PCR) test for the disease and 98% O_2 saturation by pulse oximetry (SpO_2). A 500-mg dose of acetaminophen was administered to her upon request. The sore throat and fever subsided after 5 days. Due to a neuroinflammatory reaction to viral antigens and proinflammatory mediators/immune cells as well as virus itself, headache and general malaise persisted. Considering the anti-

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inflammatory properties of these two medications, she received treatment with saiko-keishi-to (2.5 g, t.i.d.) for 7 days and minocycline (100 mg, b.i.d.) for 7 days. As a result, headache and overall malaise subsided after 3 days.

Case 2

Symptoms of a typical cold included headache, sore throat, and fever in a 48-year-old female patient. A PCR test for COVID-19 was conducted as her coworkers were COVID-19 positive. She was diagnosed as having mild COVID-19 based on the positive PCR test result and 97% of SpO_2. Fever and sore throat subsided over the clinical course. The headache persisted, and a general malaise gradually developed. These two symptoms persisted for 7 days; therefore, she was taken to our hospital. Due to minocycline's anti-inflammatory properties, she received treatment with minocycline (100 mg, b.i.d.) for 7 days. Headache and general malaise improved 4 days following minocycline medication.

Discussion

As previously mentioned, tetracyclines also have anti-inflammatory properties that, in a dose-dependent manner, reduce the production of tumor necrosis factor (TNF)-α, interleukin (IL)-6, and IL-8 (3). Several recent studies have successfully used minocycline to treat rheumatoid arthritis as evidence of its anti-inflammatory effects (5).

Tetracyclines provide neuroprotective and anti-inflammatory properties in the CNS. Additionally, tetracyclines can inhibit neuroinflammation and microglial reactivity by blocking nuclear factor kappa B signaling, cyclooxygenase 2, and matrix metalloproteinases (2). Miwa reported a long COVID-associated CNS lesion of myalgic encephalomyelitis, which was successfully treated with minocycline and had symptoms including headache and general malaise (6).

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Kampo is a traditional Japanese medicine with original theories and therapeutic methods based on traditional Chinese medicine. Kampo medications are mainly created using organic plant-based components. The components used to make saiko-keishi-to include JP Bupleurum Root, JP Pinellia Tuber, and JP Scutellaria Root (7). Saikosaponin, one of the components of saiko-keishi-to and a Bupleurum extract, has anti-inflammatory properties that inhibit proinflammatory cytokines, including TNF-α, IL-1β, IL-6 and IL-8 (4). In Japan, doctors prescribe saiko-keishi-to to treat persistent colds and flu to promote general health. Recently, two cases of COVID-19 pneumonia with headache and general malaise successfully treated using saiko-keishi-to in combination with other drugs, were reported (7).

Based on these findings, it is suggested that a minocycline and saiko-keishi-to treatment could effectively treat a CNS lesion linked to COVID-19.

In any case, clinical trials need to be conducted to better assess the optimal doses and durations and the efficacy and tolerability of this treatment before it can be adopted on a broader basis.

Conflict of Interest

No conflict of interest was declared by the authors.

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